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Outpatient Penicillin Therapy of Gonorrhea in Men

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In a previous report[1], findings were presented concerning outpatient penicillin treatment of male patients with gonorrhea. Two penicillin dosage schedules which produced fairly satisfactory numbers of cures and which were adaptable to the working hours of many clinics and offices were presented. Investigations concerning penicillin time-dosage relationships were continued with the aim of evaluating dosage schedules which would be both more effective and more readily adaptable to the needs of the private physician. It is the purpose of this paper to report the results obtained by the intramuscular administration of two 100,000 Oxford unit doses of penicillin. In group A the injections were spaced at an 8-hour interval, and in group B the period intervening between treatments was 4 hours.

The two groups of patients were comprised of young, active seamen who presented themselves at the outpatient clinic with obvious clinical evidence of the disease, confirmed by culture studies. The patients were instructed not to void for at least 2 hours before each daily posttreatment examination. Culture studies were made on the urethral secretions or on the urinary sediment and, later, on combined prostatic material and urinary sediment.

Depending on the solubility of the product used, each 100,000 Oxford units of penicillin was dissolved in 2½ to 4 cc. of distilled water and given intramuscularly into the upper and outer quadrant of alternate gluteal areas. This rather concentrated dose of penicillin did not appear to be less well tolerated than the smaller doses previously employed, and there was no evidence of toxicity.

The total of 162 patients studied was divided into two treatment groups. Group A consisted of 77 patients, each of whom received two 100,000 Oxford unit doses of penicillin with an interval of 8 hours between injections. Group B was comprised of 85 patients who received the same treatment except that the two injections were only 4 hours apart.

The criteria of cure demanded (a) that the posttreatment observation period continue for at least 8 days, (b) that there be complete subsidence of all clinical evidence of the disease by the time of release, and (c) that a minimum of 3 cultures be taken and that all posttreatment cultures be negative. In group A the average posttreatment observation period was 11 or more days; the maximum, 19 days. The average number of negative cultures was 6; the maximum, 13. In group B the average follow-up period was 12 days; the maximum, 37 days. Cultures for tests of cure averaged 6, the maximum was 12.

The results obtained will be presented separately for the patients in group A and for those in group B.

Group A (those whose injections were 8 hours apart) consisted of 77 patients, but since 22 did not return for an ample posttreatment observation period it is possible to evaluate the results in only 55 instances. Six of the 55 patients failed to respond, while 49 (89 percent) satisfied completely the demands of the criteria of cure. The 22 patients who lapsed posttreatment observation before release were clinically and culturally negative when last examined. Of the 6 failures, 3 had positive cultures on the first posttreatment day, 2 on the second day, and 1 on the third

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[1]Van Slyke, C. J.; Steinberg, S.: Outpatient penicillin treatment of gonococcic infections in males. Ven. Dis. Inform., 25: 229-232, 1944.

day. Not any of the patients of group A had complications of the disease.

Group B (injections given 4 hours apart) was comprised of 85 patients, of whom 19 lapsed the posttreatment observation requirements. Of the remaining 66 patients, 62 (about 94 percent) responded satisfactorily while 4 patients failed to be cured. Two of the failure cases had positive cultures on the second day, 1 on the third day, and 1 on the fourth day. The 19 lapsed cases were apparently cured when last seen. In group B there was 1 case of acute balanitis, which cleared promptly. One of the patients had an attack of acute follicular tonsillitis on the morning treatment was started. The penicillin therapy appeared responsible for the extremely rapid return to health.

The 10 patients in groups A and B who failed to be cured by the original penicillin treatment were retreated with smaller and more numerous doses given over a longer period of time, and all were cured. All injections of penicillin were given to this failure group at 3-hour intervals and consisted of 25,000 Oxford units administered for each of 6 injections, or 15,000 unit injections given on 10 occasions.

It was previously noted that when smaller doses of penicillin were administered over longer periods of time, although dysuria and frequency of urination cleared quickly in patients who were cured, the urethral discharge possibly tended to disappear more slowly than in patients responding satisfactorily to sulfonamide therapy. However, in the two groups treated by two 100,000 Oxford unit doses of penicillin the urethral discharge tended to disappear rapidly. On the third posttreatment day very little, if any, discharge was noted in patients who were subsequently classified as cured.

As reported in the previous paper[1], all patients are warned of the possible danger of penicillin therapy for gonorrhea masking or delaying the signs and symptoms of concomitantly acquired syphilis. Verbal warning only is not believed to be sufficient. Therefore the following mimeographed instructions are given to every patient immediately upon receiving penicillin treatment for gonorrhea:

SPECIAL INSTRUCTIONS

"The treatment you have just received may mask or delay the appearance of syphilis. Hence, it is advisable for you to have blood tests taken several times during the next two or three months.

"If any suspicious skin rash or penile sore appears, consult a doctor immediately.

"Although no evidence of disease is present, it is highly desirable for your protection and for the protection of any contact that a condom (rubber) be used until several blood tests have been taken and all of them prove negative for syphilis. This is necessary since syphilis shows up later after exposure than gonorrhea."

With the ever increasing production and availability of penicillin, and with a significant and continuing decline in cost, it appears permissible and essential at this time to question a philosophy of penicillin treatment which lays undue stress on the use of minimal amounts of penicillin to effect a cure of gonorrhea. It is possible that such dosages may promote the production and dissemination of strains of gonococci which become progressively more resistant to the action of penicillin. The use of more liberal amounts of penicillin would appear to minimize this danger, will permit a short period of treatment as demonstrated in group B (4 hour), and will permit the vast bulk of gonococcic infections to be treated expeditiously in the office of the private physician.

Summary and conclusions.—(1) Two intramuscular injections of 100,000 Oxford units each of penicillin cured 89 percent of 55 male patients when given at an 8-hour interval. When given at a 4-hour interval, 94 percent of 66 patients were cured. All failure cases were subsequently cured by smaller total doses of penicillin administered over longer periods.

(2) Although there is slight, if any, statistical significance to the difference between the cure rates reported, considerations of economy of time would appear to favor treatment over the 4-hour period.

(3) There was no evidence of toxicity, and patients appeared to tolerate the injection of 100,000 units of penicillin in-

tramuscularly as readily as the injection of much smaller amounts.

(4) The possible danger of penicillin treatment for gonorrhea masking or delaying the symptoms or findings of a concomitantly acquired syphilitic infection is recognized, and it is urged that the patient be instructed regarding this danger both by verbal and by printed instructions.

(5) It is suggested that a more liberal use of penicillin for gonococcic infections be considered as minimizing the danger of developing penicillin-resistant strains and as aiding in the rapid treatment of gonococcic infections in clinics and in the offices of private physicians.

New Jersey's Penicillin Treatment Plan for Syphilis and Gonorrhea

J. Lynn Mahaffey, M.D.[1], and Glenn S. Usher, M.D.[2]

When Mahoney first announced the successful treatment of 4 syphilitic patients with penicillin it seemed too good to be true. If penicillin were to fulfill its promise it would provide a drug which had heretofore existed only in the dreams of the most imaginative syphilologists. Nontoxic and easily administered, penicillin would provide a form of rapid treatment which would not require the services of a specialist in the field.

Some months have passed since the original observations were made by Mahoney and although we do not yet know exactly what percentage of cure rate will be attained, studies by Mahoney and others indicate that penicillin controls infectiousness quickly and that many cases are apparently cured. In gonorrhea the therapeutic value of penicillin is far more firmly established.

The peculiarities of the penicillin therapy of syphilis and gonorrhea open up possible avenues of public health application which are new to venereal disease control work. It behooves public health administrators to explore these avenues carefully and to attempt to devise means of utilizing this drug in a way which will have the greatest possible effect in reducing the attack rate of syphilis and gonorrhea.

In attempting to devise a plan, one of the most important factors was that of hospitalization. Because of the need for intramuscular injections every 3 hours, day and night, penicillin therapy requires institutional care. At the time we were considering the problem, this was true of gonorrhea as well as syphilis; experimental work on penicillin therapy of gonorrhea seemed to favor the 21-hour schedule devised by Mahoney and his coworkers.

Two approaches to the problem were possible. Existing hospitals might be utilized, or, since the low toxicity of penicillin makes necessary little more than dormitory care plus a nurse to give injections, special facilities might be provided at State or Federal expense. It was rather difficult to make a choice because each alternative offered certain advantages.

The chief advantage to be derived from the provision of special facilities is that of control. We could assure ourselves that patients would receive careful diagnostic review, adequate treatment and posttreatment observation, and adequate epidemiologic and educational services. We would not need to overcome the reluctance of hospitals to accept venereal disease patients.

On the other hand, various advantages would be gained by making use of existing institutions. The chief advantage to a general control program is the closer cooperation between the health authorities, the private physicians, and the hospital administrators brought about through the active participation of the latter groups in the program. Further, there is the practical consideration of personnel and transporta-

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tion. When we were considering this matter, the manpower shortage was a major problem, and we seriously questioned our ability to find personnel to staff a new institution and it would be difficult to provide facilities for transporting patients to one or two central points. From the point of view of the patient, the general hospital has an advantage over the special one in avoiding the labeling of a patient as one with a venereal disease. If the patient were afraid that he might encounter friends among the employees in the general hospital, arrangements could be made to send him to a similar hospital in another city. One considerable advantage would arise as a byproduct, that is, we would be providing internes—our coming generation of physicians—with a wider opportunity to observe patients with infectious venereal disease.

We chose the general hospitals and at the same time decided to develop the program in such a way as to keep as many of the advantages of the special treatment facility as possible.

We announced to physicians and hospitals an offer to reimburse hospitals for penicillin and to pay for hospitalization in the following types of patients: (1) Patients with gonorrhea resistant to one or more courses of sulfonamides (at least 20 gm.) and (2) darkfield-positive primary syphilis, secondary syphilis, syphilis with infectious relapse, cases seroresistant for 6 months after one course of penicillin, and cases of serologic relapse after penicillin treatment.

To be eligible, a patient with one of these diagnoses must be unable to afford the cost of penicillin and/or hospitalization, or be isolated by the health officer under authority of Revised Statutes of New Jersey, Section 26: 4-36.

For hospitalization, we offered to pay published ward rates, provided that this did not exceed the rates charged for patients under the emergency maternity and infant care program. The amount of penicillin used and the period of hospitalization were limited to those required to complete the recommended schedule of treatment (150,000 units and 1 day for gonorrhea, and 1,200,000 units and 8 days for syphilis).

No provision has been made for payment of the physician. The reason is that the patients are treated by nurses or internes under the orders of the hospital staff. There is nothing in the plan to prevent the patient from paying the physician for diagnosis and for test of cure. Patients who cannot afford this may be referred to clinics as heretofore, and arrangements can then be made for hospitalization under the plan. Together with this offer, there was a list of 70 hospitals, a recommended schedule of treatment and posttreatment observation, and application blanks.

Shortly after this announcement was made we discovered that some physicians were awaiting approval of their applications before starting treatment. It was emphasized that this was not necessary, as patients could be hospitalized immediately without approval. (The application blank contains a statement that after due notice we can deny the service to any physician found to be taking unfair advantage of this provision.)

In order to try to incorporate some of the control measures that would have been possible under a special facilities program, provisions for contact tracing and patient follow-up were incorporated. On the application blank, the physician must agree to arrange for the patient to be interviewed for contact information by a public health nurse of the State or local health department. We notify the nurse to be sure that this is done. Follow-up of the treated patients is provided for as follows: (1) In a case of gonorrhea, a questionnaire asking for the results of tests of cure and of blood tests for syphilis goes to the physician 1 month after treatment. (2) In a case of syphilis the physician is to be queried at 1-, 3-, 6-month and 1- and 2-year intervals. If the physician does not reply the health officer shall follow through.

We realize that we are pioneering and that the plan must go through a period of evolution. Since the inauguration of the plan, certain changes have already been made. It soon became necessary to change the basis of payment from published ward rates to ward cost rates. For this purpose we accepted the rates established by the

emergency maternity and infant care program. When the plan was inaugurated we did not have a supply of penicillin; therefore, we reimbursed hospitals at cost for the penicillin used. Now, we either replace the penicillin borrowed from the hospital depot or supply it in advance. We require that a patient with syphilis have lesions of the primary or the secondary stage, and have either a positive darkfield or a positive blood test instead of a positive darkfield in every case. In the hope of decreasing the proportion of relapses among our cases below that reported in the literature, we have added 3 injections of bismuth to the recommended schedule of therapy.

Further changes will be made as the plan matures. At present we are working on a plan to use county and municipal hospitals to supplement the overtaxed facilities of the general hospitals. Also, the shorter schedules now being used for gonorrhea will necessitate a change in the plan. The development of penicillin in oil suspension may eliminate the necessity for hospitalization and make the plan obsolete except for quarantined patients.

The plan has been well received, and there has been no serious criticism from any quarter. As yet only a small proportion of patients is being treated by this means because many physicians are not yet convinced of the value of penicillin therapy of syphilis; in gonorrhea only the sulfonamide resistant cases are treated by this means. We have not tried to overcome the reluctance of physicians to use penicillin for syphilis because no one can yet be certain of its ultimate curative effect. But we feel that the program herein described is justified by the rapid attainment of noninfectiousness with practically complete absence of danger to the patient and the consequent result in retarding the spread of the disease. Patients who relapse will be retreated either with penicillin or with arsenic and bismuth.

Conclusion.—An administrative plan is presented for utilizing general hospitals for the penicillin treatment of syphilis and gonorrhea. The hospitals have accepted the plan rather readily, as evidenced by the fact that 39 hospitals have either accepted patients or agreed to do so. Another 33 hospitals have not committed themselves one way or another, and it is believed that some of these will accept patients referred in by their staff physicians. The number of patients who have been treated so far under the plan is relatively small, and for the reasons given above we have not attempted rapid expansion. However, we believe that we are laying the foundation for a completely cooperative undertaking by uniting physicians, hospitals, and health officers into a functioning unit.

Analysis of Venereal Disease Contact Histories Received in Army Air Forces, Central Flying Training Command

E. M. Holmes, Jr., Major, Medical Corps, and Lee Chesney, Lieutenant, Medical Administrative Corps, U. S. Army

Since the early 1930's, epidemiologists have utilized questionnaires to record the results of their investigations of sexual contacts of venereal disease patients. The value of investigating the alleged contacts of a patient with venereal disease on a selective basis is well established. Venereal disease cases coming to diagnosis in dispensaries and hospitals of the Army and Navy fall largely into the category of acute early infections. The potential yield in new cases through good epidemiologic investigation of these contacts on a selective basis was obvious.

The services have been able to provide civilian health departments with identification data concerning persons who were sexually exposed to members of the Armed

Forces infected with a venereal disease. Such contact identification reports are in almost every instance reports of contacts of patients in the infectious stages of syphilis, lymphogranuloma venereum, granuloma inguinale, chancroid, or acute gonorrhea. The reporting of contacts of cases of venereal disease by the Armed Forces is in accordance with the 1940 Army-Navy-United States Public Health Service joint program for the control of venereal diseases, which was accepted by the State and Territorial Health Officers' Conference at a meeting in Washington, D. C., under the name of the Eight Point Agreement.

In the early period of the war, each Army command used its own contact report form. Many of these were inadequate and cumbersome, and the method of their distribution varied with the individual command concerned. In the summer of 1942, The Surgeon General's Office released M.D. Form 140, "History of a Venereal Disease Case," with complete and adequate instructions concerning its proper execution and distribution. It is believed that the proper usage of W.D., M.D. Form 140 has done much to systematize the transmittal of contact information, to standardize the quality of the reports, and to make the work of the component State health departments easier. To determine the effectiveness of this important adjunct to venereal disease control, a study was made of 3,270 contact histories received from stations of the Army Air Forces, Central Flying Training Command, during the period of Aug. 1, 1942 through Aug. 31, 1943.

In this 13-month period, 3,270 contact histories were received from stations of large strength served by trained venereal disease control officers, from smaller stations with untrained venereal disease control officers, and primary training detachments served only by dispensary surgeons. This number was considered as being a fair sample representative of the information being received by the health departments whose task it was to trace alleged contacts and suspect cases. The proportion of cases by disease is as follows: Syphilis 466 cases, 14.3 percent; gonorrhea 2,633 cases, 80.5 percent; other venereal diseases 171 cases, 5.2 percent.

It was arbitrarily decided that information as to identity of the alleged contact would be considered adequate if, in addition to the suspect's name, 2 or more of the other 5 pertinent identification points contained in the identification section of the history were given. These identification points are, in addition to the individual's name, the address, the telephone number, the description or distinguishing physical characteristics, the occupation, and the place of employment of the alleged contact. Data contained in the 3,270 "Contact Histories" for the period from Aug. 1, 1942 through Aug. 31, 1943, indicate that 1,604 (49.1 percent) of the 3,270 histories could be considered to contain adequate identification information (table 1).

TABLE 1.—*Data contained on 3,270 M.D. Forms 140, "Contact of Venereal Disease Case Reports" received, Hq., A.A.F.C.F.T.C., Aug. 1, 1942 to Aug. 31, 1943.*

Disease	Histories containing sufficient information to locate alleged contact			Histories containing insufficient information to locate alleged contact
	Name and 2 or more of: Home address, phone number, description, occupation, and place of employment	Name and address only	Name and description, or nickname, address, description, and others	
Gonorrhea	1,396	38	0	1,137
Syphilis	166	2	0	129
Other	42	2	0	52
Total	1,604	42	306	1,318
Percentage	49.1	1.3	9.3	40.3

In setting the standard of adequacy, perhaps the criteria were too rigid, but it was believed that with this information a trained or semitrained investigator should have little or no difficulty in locating the suspected individual. Name and address only were given in an additional 42 (1.33 percent) of the forms. Name and description, or nickname, address, and description were given in 306 (9.3 percent) of the forms. Thus, it was considered that out of 3,270 histories, 1,952 (59.7 percent) contained sufficient information to warrant the health officer's assigning an investigator to search for the individual named. Data contained in 1,318 histories in this study were considered as inadequate; these histories contained insufficient information to warrant field investigation.

Less than 10 percent of these histories listed more than 1 sex partner, which indicates that the venereal disease control officers of the Army are in many instances content with eliciting 1 contact per case. Considering that it is only through the prompt investigation of all contacts and the bringing them to examination and treatment, if necessary, that the overwhelming reservoir of infection in the population at large can be reduced, it is essential that the medical officers increase their efforts to obtain adequate epidemiologic data from their cases.

On the contact history form, name and address of place of exposure is listed, and under procurement history space, the listing of name and address of place of procurement is provided. By the tabulation of accumulated reports geographically, even histories not listing the contact can be utilized to localize places of procurement and exposure. Often such data upon tabulation indicate that a specific area of a given city may be a source of danger to the Armed Forces. These data tabulated by place of procurement and exposure may be submitted by the surgeon to the health authorities for appropriate action, or by the provost marshal to the police authorities. If the civilian authorities are reluctant to take sufficient measures to remedy the condition, recourse to the "Off Limits" proceeding may be justified on a basis of such data for it is an established practice that areas where the prevalence of communicable disease is high be quarantined, and that persons be restricted from entering such danger areas.

Twenty-three and five-tenths percent of the patients alleged that their exposure occurred in their consort's home (table 2), 33.2 percent that their exposure occurred in hotels, and 14.7 percent stated that their contact occurred in automobiles. Twenty-eight and six-tenths percent of the patients reported that their exposure occurred in rooming houses, parks, tourist homes, and brothels. Information from these reports revealed that hotels, rooming houses, and tourist camps were alleged as place of exposure and contact by 1,376 (42.1 percent) of the patients. It becomes apparent that this information, more definitively broken down by cities, specific hotels, and taverns, if made available to the health department, can be utilized to focus the attention of police departments and hotel men's associations on this aspect of the problem.

TABLE 2.—*Alleged source of infection and places of exposure, tabulated from M.D. Form 140, "Venereal Disease Contact Reports" received, A.A.F.C.F.T.C., during the period Aug. 1, 1942 to Aug. 31, 1943.*

Place of contact	Wife	Pick-up	Friend	Brothel prostitute	Call girl	Street-walker	Unknown	Total	Percent
Home	160	305	275	3	2	25	1	771	23.5
Automobile	3	322	133	2	0	23	1	484	14.7
Hotel	14	668	232	35	80	57	1	1,087	33.2
Brothel	2	26	3	132	1	9	0	173	5.3
Tourist camp	2	108	40	5	0	4	0	159	4.9
Rooming house	0	96	21	3	3	7	0	130	4.2
Tavern	0	5	2	0	0	0	0	7	0.2
Other, unknown	0	302	86	4	2	19	46	459	14.0
Total Number	181	1,832	792	184	88	144	49	3,270	100.0
Percent	5.5	55.9	24.4	5.6	2.7	4.4	1.5	100.0	

With such information, health departments, in cooperation with the Army, can achieve rigid enforcement of antifacilitation regulations by hotel associations. Alcohol beverage control boards can be stimulated to enforce their regulations and thus reduce the number of pick-ups in taverns, barrooms, and beer parlors.

M.D. Form 140 classifies type of contact as wife, pick-up, friend, brothel prostitute, call girl, streetwalker, and unknown. Data from 3,270 histories contained the following information: 181 (5.5 percent) of the patients stated that they had acquired infection from exposure with their marital partner. This number is consistent with previous epidemiologic reports and analysis of Army M.D. Forms 140. Pick-ups and casual acquaintances were named as contacts by 1,832 (55.9 percent) of the patients while 792 (24.4 percent) named a friend as their only contact. Thus, in 2,624 (80.3 percent) of these reports, the individuals stated that they were exposed by casual picks-ups, friends, or acquaintances. The brothel prostitute functioning in a house of prostitution was reported as a contact on 184 (5.6 percent) of the forms. Call girls and streetwalkers, alleged to have been paid, accounted for 232 (7.1 percent) of the reports. The fact that only 416 (13.7 percent) stated that they had paid for their exposure is of importance when compared with 2,624 (80.3 percent) who stated that they acquired their infection as a result of sexual exposure with casuals, charity girls, and friends.

In summary, it is believed that until such a time as better contact data are provided by medical officers the reservoir of venereal disease infection in civilian communities will remain an obstacle in venereal disease control.

Further, it is believed that contact histories with incomplete data can be utilized, if tabulated on a geographic basis, to focus attention on areas of communities where exposure and procurement take place.

Conclusion.—1. An analysis of 3,270 M.D. Forms 140, "History of a Venereal Disease Contact," revealed that only 59.0 percent contained sufficient information to permit the cooperating State and local health departments satisfactorily to investigate the suspect case, evidencing the fact that there is a need for more thoroughness in history taking by medical officers.

2. Less than 10 percent of the case histories reported more than 1 sex partner per case, which can be considered as presumptive evidence that medical officers in many instances are content with 1 contact per case.

Acknowledgment is made of the cooperation and interest of Col. E. F. Harrison, M.C., Surgeon, AAFCFTC, Randolph Field, Tex.

DIAGNOSIS

Acute yellow atrophy of the liver in early syphilis: a case report with summary of the literature. Martha F. Leonard. Am. J. M. Sc., Philadelphia, 208: 461–470, Oct. 1944.

The author states that acute yellow atrophy associated with acute syphilis is not different clinically from that of other causes. Beginning insidiously like a benign hepatitis, often hepatomegaly, it may or may not be accompanied by fever, malaise, muscle pains, nausea, vomiting, or pruritis. A sudden turn for the worse with psychic and neurolgic disturbances—headache, restlessness, disorientation, delirium, hyperactive reflexes, convulsions—will be followed by coma and death. The liver will shrink rapidly in size during the latter phase, crystals of tyrosine and leucine may appear in the urine, and frequently the patient has a slight fever and a pungent odor, suggestive of acetamide.

The case of a 15-year-old white girl is reported. She gave a history of genital lesion 3 weeks before admission to the hospital. This disappeared within 3 or 4 days to be followed by lesions on the face, arms, and legs, darkening of the urine, jaundice of the skin and eyes, malaise, slight fever, anorexia, and nausea. Examination revealed a generalized papular eruption, general lymphadenopathy, and inflammation of the tonsils. Liver and spleen were not palpable. The vulva showed inflammation and edema with small ulcers,

and there was a profuse vaginal discharge. A pungent, mousy odor was noticeable in the patient's room. Darkfield, Wassermann, and Kahn tests were strongly positive. Between November 2 and 8, the patient received 3 injections of mapharsen (0.015 gm, 0.03 gm., 0.04 gm.) and 2 of bismuth (0.13 gm., each). The patient was afebrile, skin lesions and ulcers of the vulva were subsiding, but the jaundice persisted. The patient became suddenly worse, with stupor, hyperactive reflexes, clonus, positive Babinski reflex, and dilated pupils. She died November 17.

Autopsy showed typical acute yellow atrophy of the liver with cerebral edema and no hemorrhage of the brain. The author doubts that death was due to arsenic, since only the last dose was of therapeutic size, and suggests that the occurrence of jaundice simultaneously with the secondary syphilitic eruption indicates that it was syphilitic in origin. She concludes that clinical evidence of the deleterious effect of arsenical therapy in the jaundice of early syphilis is incomplete, that reports of prompt relief of symptoms by specific therapy favor its use, but warns that one must bear in mind the general tendency to fail to report unfavorable cases.

Epidemiological study of lymphogranuloma venereum, employing the complement-fixation test. Paul B. Beeson and Edward S. Miller. Am. J. Pub. Health, New York, **34**: 1076–1082, Oct. 1944.

Complement fixation tests for lymphogranuloma venereum were done on 397 Negro and 348 white clinic patients at Grady Hospital, Atlanta, and the results analyzed according to race, age, and sex.

Among the adult Negro group, 39.7 percent of female patients and 44.8 percent of male patients gave positive reactions. There were only 6 positive reactions among 116 Negro children under 14 years of age. Of the adult white group, the incidence of positive reactions was 12.1 percent for female patients and 11.6 percent for male patients; there was 1 positive reaction among 58 white children under 14 years of age. The incidence of positive reactions was approximately the same in all age groups beyond 40 years. The persistence of an immune reaction in age groups where sexual contacts are less frequent suggests the possibility that the virus persists in the body, providing continued antigenic stimulus.

Comparisons were made of the complement fixation reaction in 37 newborn Negro infants and their mothers. It was found that immediately after birth the reaction in the infant's serum was the same as that of the mother. Nine infants who had given positive reactions were retested 2 to 4 months later and their reactions were negative. It appears, therefore, that a positive test at birth is due merely to the passive transfer of antibodies from the mother.

The error introduced by the fact that infection with other members of the lymphogranuloma-psittacosis group of viruses will give rise to positive complement fixation tests for lymphogranuloma venereum cannot be assessed. It is not likely, however, that the prevalence of infection by the other agents in this group is sufficiently great to distort markedly the picture of the prevalence of lymphogranuloma venereum.

The results of the Kahn test for syphilis in this group are reported. The incidence of positive Kahn reactions in the adult Negro group was 33.0 percent for female and 32.1 percent for male patients. In the adult white group, the incidence was 6.9 percent for female and 14.7 percent for male patients. Analysis of the data shows that the similarity in incidence of positive tests for syphilis and lymphogranuloma venereum was not due to the same persons giving positive tests for both diseases.

The authors believe that the high incidence of positive tests for lymphogranuloma venereum in individuals with syphilis and other venereal diseases is due to actual associated lymphogranuloma infection, even in the absence of clinical signs.

Symptomatic neurosyphilis. A clinical survey. Harry C. Solomon, J. E. Moore, Paul A. O'Leary, John H. Stokes and Evan Thomas. Bull. U. S. Army M. Dept., Carlisle Barracks, No. **81**: 55-64, Oct. 1944.

The symptoms of syphilis of the nervous system may simulate all forms and varieties of neuropsychiatric disorder. Therefore, in disorders suggesting organic involvement of the nervous system, whether the symptoms or signs be physical or mental, neurosyphilis must be ruled out before making any other diagnosis.

Neurosyphilis is divided into two main categories: (1) Meningovascular neurosyphilis, and (2) parenchymatous neurosyphilis. The clinical distinction between the two is of importance, for meningovascular neurosyphilis produces little or no irreparable damage to nerve cells, except secondarily by interruption of blood supply, and trivalent arsenicals and bismuth are more beneficial than in cases of parenchymatous neurosyphilis.

The symptoms of neurosyphilis are directly dependent on the locus of involvement and the extent of the lesion. As any blood vessel may be damaged in meningeal neurosyphilis, leading to thrombosis and occasionally rupture, every known syndrome of nervous system disease or disorder may develop. In the majority of cases of parenchymatous neurosyphilis the frontal lobes are predominantly involved, giving rise to the syndrome of general paresis. In the cord, the posterior roots and posterior columns of the thoracolumbar cord are most commonly involved, producing the clinical picture of tabes dorsalis.

Clinical manifestations of neurosyphilis —syphilitic meningitis, meningovascular neurosyphilis, tabes dorsalis, general paresis, vascular neurosyphilis, congenital neurosyphilis—are described.

In tabes dorsalis, symptoms which have existed for some time before treatment was instituted persist despite the return of the spinal fluid to normal. This has led to speculation concerning the mechanism of the symptoms in tabetic neurosyphilis, and indicates that they are not due in their entirety to the activity of spirochetes. A late complication of tabes dorsalis is joint destruction, known as Charcot's joint, which often occurs in patients who have normal spinal fluid reactions and evidence of complete arrest of the other tabetic symptoms.

The authors point out that the galaxy of symptoms of general paresis is too frequently diagnosed as psychoneurosis. In untreated patients, about one-half die within 2½ years of the onset of mental symptoms, and almost all die within 5 years. The prognosis of general paresis under treatment is, in the majority of cases, an arrest with some residual defect, the extent depending upon the amount of damage occurring before treatment became effective. When the physical state of the patient permits, fever therapy as well as chemotherapy should be instituted.

Tropical diseases of the skin. Howard Fox. New England J. Med., Boston, 231: 482–485, Oct. 5, 1944.

Yaws and pinta are two tropical diseases in which cutaneous manifestations constitute either the entire clinical picture or an important part of it, and which are caused by organisms morphologically identical with Treponema pallidum.

The geographic distribution of yaws includes parts of equatorial Africa, many islands of the Pacific, Burma, Thailand, some islands of the West Indies, and tropical parts of South America. There are 4 features that yaws and syphilis have in common: (1) Causative organisms are morphologically identical; (2) both diseases give the same serologic reactions; (3) both yield to arsphenamine and allied drugs and to bismuth, and (4) in both, the late destructive tertiary lesions are clinically indistinguishable. One striking difference between yaws and syphilis is that in yaws the infection is usually extragenital.

It is noteworthy that after prolonged infection there is a complete cross immunity between the two diseases. It has been observed in the island of Guam that most of the natives are immune to syphilis, since in childhood they have been infected with yaws.

The greatest incidence of pinta is found in Colombia and the southern half of the Republic of Mexico; a survey made a few years ago in Mexico disclosed over 270,000 cases.

TREATMENT

The treatment of early and latent syphilis. Harry Eagle. J. A. M. A., Chicago, **126**: 538–544, Oct. 28, 1944.

This paper presents a preliminary analysis of the results among 4,823 patients treated for syphilis in 9 to 12 weeks with triweekly injections of mapharsen. Two-thirds of the patients were given concomitant weekly injections of a bismuth compound. Primary or secondary syphilis was present in 3,394 of the patients, latent syphilis in 1,190, and recurrent or relapsing syphilis in 159. Forty percent of the total were white, and 60 percent Negro; 53 percent were male, and 47 percent female.

Toxic reactions were divided into 3 groups. Minor subjective reactions occurred in 16 percent of the patients and approximately 1.5 times more often in women than in men. In 106 patients a syndrome was observed suggestive of sensitization to mapharsen. Symptoms among these consisted of fever, rash, vomiting, headache, conjunctivitis, and facial edema. Serious toxic reactions occurred in 39 patients. Among these there were 2 cases of toxic encephalopathy, 7 of arsenical dermatitis, 4 of nephritis, 5 of blood dyscrasia, and 21 of jaundice. Seventy percent of the sensitization reactions and 75 percent of the serious reactions occurred in the second to fourth weeks of treatment. Four deaths occurred in the series, 2 from nephritis, 1 from toxic encephalopathy, and 1 from jaundice. It was felt that 2 and possibly 3 of these might have been prevented.

In evaluating therapeutic results, the cumulative percent of failures was calculated by a modified life table technic. Included as treatment failures were patients showing infectious relapse, clinical or serologic evidence of central nervous system involvement, serologic relapse, or a persistently positive blood test at a more or less stationary level 1 year after the beginning of the treatment. It was found that mapharsen alone gave uniformly poor results, whereas the addition of only 5 injections of bismuth to the smaller amounts of mapharsen significantly decreased the percentage of failure. When an average of 9 injections of bismuth was added to the larger amount of mapharsen, the cumulative percentage of treatment failure 70 weeks after beginning treatment fell to 9.3, and 82 percent of the patients were seronegative, with the remainder of the cases pending. The 2 drugs are apparently not merely additive but actually synergistic in their therapeutic effects.

Results among patients with latent syphilis were consistent with those obtained with routine standard methods of treatment.

The action of penicillin in late syphilis, including neurosyphilis, benign late syphilis and late congenital syphilis: Preliminary report. John H. Stokes, Thomas H. Sternberg, Walter H. Schwartz, John F. Mahoney, J. E. Moore and W. Barry Wood, Jr. J. A. M. A., Chicago, **126**: 73–80, Sept. 9, 1944.

The cases discussed in this paper were drawn from 8 clinics engaged, under the Penicillin Panel, in the study of the effect of penicillin on late syphilis. The 182 cases were observed from 8 to 214 days after penicillin therapy was begun. The authors made the following tentative observations:

The lesions of benign gummatous syphilis of skin and bones healed under a dosage of approximately 300,000 units in 12 to 46 days. Irrespective of the system used and in all types of syphilis, penicillin caused reduction of syphilitic reagin titer in the blood in from 50 to 60 percent of late cases. An initial "Herxheimer"-like or provocative rise was observed in about 20 percent of the cases. Only 5 seroresistant cases were treated; 1 negative, 4 improved.

The abnormal spinal fluid in neurosyphilis was improved to some degree in 74 percent of 107 patients of whom 33 percent showed definite improvement. The commonest change was a drop in cell count and total protein occurring in 67 per-

cent of cases. One spinal fluid was rendered normal.

Symptoms improved in neurosyphilis as follows: In 30 cases of simple demented paresis, 80 percent improved to some degree; nearly half improved 50 percent or more. In deteriorated paresis, 2 out of 10 improved 75 percent; one-fifth of 14 cases of tabes dorsalis improved 50 percent or more. Of 7 patients with primary optic atrophy, mostly advanced cases, none were made worse and 1 improved. In meningovascular neurosyphilis, 40 percent improved 50 to 75 percent.

Interstitial keratitis presented rather equivocal though at times dramatically favorable results. Two cases of optic neuritis improved, the second case 100 percent on retreatment. Two cases of iritis improved 100 percent at the start, but 1 relapsed and did not respond to retreatment. Two cases of eighth nerve deafness gave equivocal results.

Attempted statistical evaluation suggested that in late syphilis, especially neurosyphilis, smaller doses have good effects which may perhaps be improved by repetition, as compared with the effects of initial larger dosage.

Previous treatment of syphilis by older methods did not appear to prepare the patients for superior results with penicillin. Reactions to penicillin as such were few and not serious.

In the discussion, Barksdale reported on 161 patients with syphilis treated with penicillin by the Navy, Leifer on 116 cases treated at Fort Bragg, and Ellis on penicillin used in New Zealand and Corpus Christi. Wile and Moore both stressed the necessity of not being too optimistic in regard to therapy with penicillin.

Intensive arsenotherapy. A. Benson Cannon, Jerome K. Fisher, Juan J. Rodriguez, Guila F. Beattie and Eugenia Maechling. J. A. M. A., Chicago, 126: 544–550, Oct. 28, 1944.

The authors studied the results of the treatment of 332 cases of early syphilis with massive doses of arsphenamine given by the syringe method 3 or 4 times daily for 5 or 6 days. All the patients were men, chiefly young and healthy, and all of them were hospitalized for treatment. Seven different variations of the original plan of treatment were used, the total dosage ranging from 1.5 gm. of the drug in the beginning to 4.4 gm. in the latter part of the program.

A detailed analysis of the outcome of the treatment and of the reactions, together with observations of results, is given. Of the 332 patients treated, 178 were followed for a period of from 6 months to 3 years, and the evaluation of treatment results is based on these cases. In this group, 118 (66 percent) were clinically and serologically negative with normal spinal fluid reactions; 57 had unsatisfactory outcomes, 36 of which were mucocutaneous relapses with recovery of spirochetes. Severe reactions occurred in 12 patients, 1 of whom died.

A daily blood arsenic determination was made on each patient. The findings indicate that there was a retention of arsenic long after cessation of treatment, that all reactors showed a greater retention of arsenic and for a longer period than did nonreactors, and that the more arsenic received the greater the retention.

The authors conclude that treatment of early syphilis with arsphenamine by the multiple syringe method over a period of 5 or 6 days is ineffective, dangerous, expensive, and impractical. They are convinced that any such 5- or 6-day treatment plan with arsphenamine, using the multiple syringe method, should be followed by additional therapy of a heavy metal, fever, or both.

Toxic effects of arsenical compounds as administered in the United States Navy in 1943, with special reference to arsenical dermatitis. T. J. Carter, Wesley M. Chambers and Laura T. Anderson. U. S. Nav. M. Bull., Washington, 43: 787–799, Oct. 1944.

During 1943, medical officers of the U. S. Navy administered a total of 245,331 doses of arsenicals, and reported the occurrence of 49 untoward reactions. Of these toxic reactions, there were 26 cases of arsenical dermatitis, a ratio of 1 to every 9,436 doses,

and 1 fatality. Of interest in connection with a review of the causes of arsenical dermatitis are the instances in which premonitory signs were noted. They tend to indicate the necessity for careful examination and questioning of each patient before administration of an arsenical.

Tables are presented showing, for each type of arsenical preparation used, the number of doses administered and the number of reactions classified as mild, severe, and fatal. These data are given for 1943 and for the 19-year period, 1925-1943. For the period 1925–1943, a table is presented showing the number of reactions, classified according to type. Case histories are given illustrating the various types of reactions encountered in 1943.

Penicillin in the prevention and treatment of congenital syphilis. Report on experience with the treatment of fourteen pregnant women with early syphilis and nine infants with congenital syphilis. J. W. Lentz, Norman R. Ingraham, Jr., Herman Beerman and John H. Stokes. J. A. M. A., Chicago, **126:** 408–413, Oct. 14, 1944.

Twelve pregnant women with symptomatic early syphilis and 2 with early latent syphilis, and 9 infants with early congenital syphilis were considered in this study; none had received any type of antisyphilitic therapy prior to treatment with sodium penicillin. The maximum period of observation at the time these data were analyzed (June 29, 1944) was for the mother, 7½ months, and for the newborn infants, 3 months; for the infants with congenital syphilis, the period of observation was about 4 months. Observations were made by members of the University of Pennsylvania Penicillin Panel. Seven of the mothers had not been delivered at the time of this report.

The infants of the 7 mothers who were delivered were all apparently normal at birth. Darkfield examination of the umbilical vein was negative in 5 infants, and not performed in 2. Roentgenograms of the long bones performed in 4 infants at birth and repeated 6 weeks or later were all normal. Three of the infants had positive cord and neonatal blood serologic tests with quantitative titers either equal to the mother's or lower; the serologic tests became normal in less than a month. In 4 infants, the blood serologic test was negative at birth and remained seronegative at the time these data were compiled. Only 3 of the mothers became seronegative during the period of observation—one patient was seronegative 95 days after penicillin therapy and 47 days prior to delivery, another had not reached term but was seronegative 77 days postpenicillin and remained so for 2 months, and the third patient was seronegative 69 days after delivery. In no instance was treatment instituted prior to the midpoint of the pregnancy or in the month immediately preceding term.

Ten of the women received 25,000 Oxford units of penicillin (a total of 1,200,000 units), and 4 women, 50,000 units (a total of 2,400,000 units), administered intramuscularly every 4 hours for 8 days. Threatened abortion in 2 patients was the only reaction; one occurred 18 hours and the other 48 hours after starting penicillin therapy. The drug was discontinued, but was resumed in full dosage within 24 hours without recurrence of symptoms. The findings indicate that it is advisable to reduce the penicillin dosage by three-fourths to one-half during the first 36 to 48 hours of treatment of the syphilitic pregnant woman.

Of the 9 patients with early congenital syphilis, a complete record was available for only 3. These infants had relatively high blood serologic titers initially, dropping to normal in 1, and to relatively low levels in 2. Two infants who showed definite roentgenographic changes of syphilitic osteochondritis and periostitis resumed approximately normal bone development.

Six of the 9 infants received a total dosage of between 16,000 and 19,000 units of penicillin, per pound of body weight, every 4 hours for 8 days. Three infants received 2,935, 10,631 and 11,111 units per pound of body weight, respectively. The only definite reaction was dyspnea and cyanosis in 1 patient, necessitating supportive treatment and discontinuance of the drug for 24 hours. Penicillin was re-

sumed in full dosage without recrudescence of symptoms. The reaction occurred after the patient had received 19,000 units of penicillin in the first 48 hours of treatment.

One of the 14 pregnant women who was treated with 1,200,000 units of penicillin developed infectious relapsing lesions prior to delivery, 122 days after penicillin therapy. Darkfield-positive skin lesions appeared in one of the congenitally syphilitic infants 6 months after penicillin therapy had been started, the blood titer rising to 32 units. The infant remained seropositive. The mother, who was receiving treatment with phenarsine hydrochloride and bismuth subsalicylate, showed no evidence of open lesions at the time of relapse in the infant. This was considered a penicillin failure and the infant was retreated with penicillin.

The authors conclude (1) that these preliminary results indicate that "cure" or suppression of the infection takes place in a number of the mothers; (2) that miscarriage, stillbirth, and neonatal death are averted, and (3) that the infants are born apparently healthy. It must be emphasized, however, that the period of observation for mother and child has not been long enough to be certain that they have been cured by the dosages employed. Grossly infected, syphilitic infants may be injured by the injudicious use of penicillin; treatment should be approached with extreme caution, with reduced dosage and emphasis on proper general pediatric care.

The clinical use of penicillin in genitourinary infections. Gershom J. Thompson. J. A. M. A., Chicago **126:** 403–407, Oct. 14, 1944.

Five hundred patients with gonococcic infection of the urethra or its adnexa were treated with penicillin by several methods.

The highest percentage of cures resulted from intramuscular injections of 20,000 units of penicillin, administered every 3 hours for 5 doses (a total of 100,000 units over a 12-hour period). Out of a total of 366 patients treated by this method, there were 8 failures (2 percent). However, these failures were cured by subsequent treatment with penicillin. In no case did the infecting organism prove penicillin-resistant.

Culture of the urine was obtained 12 to 18 hours after conclusion of treatment, and culture from the prostatic fluid, 48 hours after the first injection of penicillin; in practically all instances these cultures were negative.

Studies of the purulent urethral secretion, the sediment from the centrifuged urine and the prostatic secretion of Gram's stain were reliable methods in determining clinical response to treatment. In many cases, the gonococci disappeared from the urethral secretion within 2 hours.

The dramatic cessation of the purulent urethral discharge is the most impressive point in penicillin therapy. In some cases, a small mucopurulent or mucous drop can be expressed from the urethra each morning for several days, or as long as a week, but should not be considered as cause for retreatment.

The author is of the opinion that although this group of patients was followed for relatively short periods, if the culture of the prostatic secretion is negative for 48 hours after treatment, it will usually remain negative.

One important point in considering results of penicillin therapy is that at present there is no great assurance that an ampule of penicillin contains the exact amount as stated on the label. The author feels that many of these patients received much more than 100,000 units. This is not the fault of the manufacturer; rather, it can be attributed to the inexact methods of assay which are now available.

Acute gonorrheal epididymitis, prostatitis, or seminal vesiculitis was observed in only 10 cases in this series and 5 of these received an additional 100,000 units of penicillin. Gonorrheal arthritis was observed in 6 cases, but did not respond to penicillin therapy, although the concomitant urethral and prostatic infections responded to treatment.

There were no serious toxic reactions. The author concludes that treatment with penicillin is so devoid of toxic reaction that there is no reason to outline difficult schedules or to use complicated methods. The

physician need not be fearful of using too much of the drug.

Sulphonamide resistant gonorrhoea. Editorial. J. Roy. Army M. Corps, London, 82: 283–285, June 1944.

There is no doubt, the author states, that sulfonamide resistance in treatment of gonorrhea is becoming more and more common, and this may also become true for penicillin. If some of the strains of gonococci now prevalent in Italy and other European countries are introduced into England, incalculable harm may be done.

Assuming that the drugs are of standard potency, the explanation of sulfonamide resistance must lie either in the organism, in the patient, or in the effect of one upon the other. In vitro experiments have shown that some strains are more resistant than others, some being completely unaffected by the drug; some strains seem to be naturally resistant while others acquire resistance, possibly as a result of sublethal doses of the drug. Assuming that a given strain has acquired resistance, the question arises as to whether it will remain resistant when transferred to another host.

It is clear that in Sicily and Italy strains exist which are extremely resistant, especially when in British, American, and Canadian soldiers; there is no definite evidence that they are so resistant in Italians or Germans. Various suggestions as to the cause of this are not adequate. If it is assumed that strains of gonococci are either sulfonamide-sensitive or sulfanilamide-resistant, it would follow that the more people are treated with sulfonamides, the more the sensitive strains are killed off and the more the relatively resistant strains survive. If this goes on, there is the gloomy prospect of all prevalent strains of the gonococcus being sulfonamide resistant.

Partially sulfonamide resistant gonorrhea can usually be cured with a little ingenuity. If a single course does not effect cure, irrigations often do so. If a second course is necessary, a different sulfonamide compound should be used. Completely resistant gonococci present a difficult problem. Probably 95 percent of the cases will clear up with penicillin, but this drug is not available. Artificial hyperpyrexia, especially if chemotherapy is used concomitantly, will cure most of these cases. The most commonly used method is the intravenous injection of typhoid vaccine; this is inexpensive and can be given in any well-equipped hospital.

Sulfonamide resistant gonorrhea is no longer a problem to be treated by theories; it must be met quickly before the dangerous strains get a firm grip on the human race.

Renal damage from sulfonamide compounds. Editorial. J. A. M. A., Chicago, 126: 302–303, Sept. 30, 1944.

Shortly after the sulfonamide compounds came into general use, physicians recognized that the kidney may be damaged in the course of therapy with these drugs. Two types of renal complications were observed: (1) Those due to mechanical obstruction of the pelves, the ureters, and the renal tubules by crystals of the sulfonamide compounds, and (2) those due to toxic lesions of the kidney without obstruction. Combination of the 2 forms has likewise been described. In addition to tubular necrosis, which is the usual expression of damage by toxic substances, instances have been observed in which interstitial tissue reaction with necrosis was also present. Murphy and his associates observed 1 such instance in the series reported by them. They feel that this type of reaction is probably an expression of severe idiosyncrasy on the part of the renal tissue to the drug. This inflammatory response was also seen in tissues outside of the kidney represented by giant cells and perivascular granuloma-like cell accumulations suggesting a similarity with periarteritis nodosa and similar lesions. The hepatic damage observed in these cases is probably related to the nephrotoxic complications.

Study of clinical data of 14 patients with renal insufficiency following use of sulfonamide compounds in relation to postmortem observations on 13 revealed that the quantity of the sulfonamide compound administered and the drug level in the blood appeared to be unimportant in producing the renal damage. As much as 41 gm. and as little as 0.6 gm. were responsible for fatal

renal injury. In a few of their cases, deposits of crystals of the drugs in the urinary tract causing some degree of mechanical obstruction were found associated with the nephrotoxic lesion; this was not the rule, however, as in most of the cases the nephrotoxic lesions were independent of mechanical blocking.

Microscopic alterations in tubular epithelium were observed, which varied from simple degeneration to tubular necrosis and intense inflammatory reaction outside the nephron. The investigators feel that these tubular lesions represent degrees in the severity of one process rather than different kinds of response. The study failed to correlate the clinical features with the specific site for the renal tubular damage.

Of the numerous toxic complications caused by sulfonamide compounds, that affecting the kidney is most serious. Fortunately these complications are comparatively uncommon. The mechanical type of complication, particularly that outside the kidney, in the pelvis and the ureter, responds best to therapeutic measures. When, however, obstruction occurs within the kidney a cure is not easily accomplished, although retrograde lavage should always be done and the drug discontinued. Precipitation of the sulfonamide compound is the etiologic factor in these obstructions. Precipitation should be prevented as far as possible by the administration of adequate fluids and maintenance of an alkaline urine.

Venereal disease and flying personnel. Robert Dyar and Julius R. Scholtz. J. Indiana M. A., Indianapolis, 37: 435–438, Sept. 1944.

Venereal disease must be considered from 3 standpoints as it affects the ability to perform flying duty: (1) The possible effects of the disease on normal physiology; (2) the effects on the occurrence of disturbances characteristic of flight, and (3) the possible accentuation of minor pathologic changes, ordinarily below the clinical horizon, under flying conditions.

Lymphogranuloma venereum and granuloma inguinale are disqualifying for any type of military service. When such infection is acquired after induction during flying training, or after the individual is qualified for flying, disposition varies, depending upon extent of the infection and early response to treatment, and upon whether the individual has had long service and a high degree of training.

Ducrey infections, uncomplicated, are acceptable for general military service since the majority of cases respond readily to sulfonamide therapy and are cured within a few weeks. If such infection occurs in individuals undergoing flying training, or on active flying duty, they are grounded during the course of treatment because of the drugs which are used.

Gonorrhea, uncomplicated, is also acceptable for general military service since, in most instances, it can be cured in a few weeks with sulfonamide therapy, after which the individual is physically qualified for any type of military duty. While under treatment, the individual is temporarily disqualified for flying.

The presence of syphilis of the central nervous system, cardiovascular system, or viscera, and any clinically active syphilis—other than primary and secondary—are disqualifying for induction into the Army.

Individuals with primary, secondary, and latent syphilis, in training or applying for training, are not qualified for flying duty or training until they have completed a 6-months' course of treatment and a 6-months' observation period. The spinal fluid must be negative at the end of treatment. The applicant can then be accepted for training if waiver is granted by the Commanding General of the Army Air Forces. Individuals with early syphilis and latent syphilis (spinal fluid negative) who are already qualified (trained) for full flying status are suspended from flying duty for an initial minimum treatment period of 4 weeks. Only those considered well-adjusted to treatment and free from all clinical signs and symptoms of active syphilis at the expiration of the suspension period are considered for flying duty. A 24-hour period subsequent to an arsenical injection must elapse before individuals undergoing treatment can be returned to flying duty. Examination is made by the flight surgeon

following each arsenical injection, immediately prior to resumption of flying duty. Present Army Air Force regulations provide that individuals required to perform flying duty will be grounded during and for 6 days following the last dose of a sulfonamide compound administered systemically.

Penicillin has almost completely changed the perspective in regard to gonorrhea in flying personnel. Since early in 1944, penicillin has been available for initial treatment of gonorrhea, and air crews enroute to overseas destinations have been able to remain intact, without the delay which formerly resulted with sulfonamide therapy.

LABORATORY RESEARCH

The absorption and excretion of penicillin following continuous intravenous and subcutaneous administration. Lowell A. Rantz and William M. M. Kirby. J. Clin. Investigation, Boston, 23: 789–794, Sept. 1944.

The authors studied the concentration of penicillin in blood and urine during the administration of this agent by continuous intravenous and subcutaneous drip methods. Both turbidimetric and dilution methods of determination were employed, substantial agreement being found between the two.

In 7 patients under rigidly controlled conditions of continuous intravenous administration there was found an approximately linear relationship between the rate of administration and the blood concentration, and between the rate of excretion and the blood concentration. The rate of excretion was approximately equal to the rate of administration. The plasma clearances of penicillin at the lowest and highest rates of administration were comparable, suggesting that the maximum rate of tubular excretion of this substance had not been reached. The differences in the rate of urinary flow were not associated with variations in the plasma clearance of penicillin.

In a group of 6 febrile patients, it was found that the average plasma clearance was approximately 50 percent greater than in afebrile patients.

Determinations of the plasma concentration of penicillin were made in an unspecified number of patients receiving routine treatment by either intravenous or subcutaneous routes, but under less rigidly controlled conditions. It was found that when penicillin was administered subcutaneously, the plasma levels were about 50 percent lower than when administered intravenously.

Methionine protects against mapharsen liver injury in protein-depleted dogs. J. P. B. Goodell, P. C. Hanson and W. B. Hawkins. J. Exp. Med., Baltimore, 79: 625–632, June 1944.

This study presents evidence that oral administration of methionine affords protection against liver damage following large doses of mapharsen given to protein-depleted dogs. Dogs kept for several weeks on a very low protein diet were divided into 3 groups. Group 1 consisted of animals unprotected by methionine, group 2 of those protected by the drug, and group 3 of those which were alternately protected and unprotected.

Since study of the physiologic function of the liver injured by arsenical poisoning is a better index of the degree of dysfunction than histologic examination of the organ, the animals were not sacrificed at the height of the injury, but were judged by the changes in the icterus index. The authors conclude that depletion of body protein stores by means of low protein diet or plasmapheresis causes greater susceptibility to liver injury by mapharsen. Normal dogs can tolerate mapharsen in doses of 0.006 to 0.008 gm. per kilogram, whereas protein-depleted dogs developed liver injury with jaundice following doses of 0.002 to 0.0025 gm. per kilogram. Dogs given 2 to 4 gm. of methionine orally 20 to 24 hours prior to administration of mapharsen will

tolerate 0.0045 gm. per kilogram without developing icterus. Methionine given intravenously in 1 gm. doses immediately prior to the mapharsen was not adequate protection.

Artificial fever chemotherapy. 1. Bismuth excretion studies. H. Worley Kendell, R. M. Craig, G. X. Schwemlein and H. C. S. Aron. Arch. Phys. Therapy, Chicago, **25:** 593–598, Oct. 1944.

This study is an investigation of urinary bismuth excretion in patients undergoing fever-chemotherapy for early syphilis undertaken in order to learn whether routine methods in operation produced the therapeutic level of the drug and if not, whether that level could be achieved without danger to the patient. The authors accepted 2 mg. as the minimum daily excretion of bismuth necessary for therapeutic efficiency.

To a group of 40 patients was administered 1.75 mg. mapharsen per kilogram of body weight with 8 hours of fever maintained at the level of 106.0° F. (rectal), with 2 cc. of oil-insoluble bismuth given intramuscularly 16 hours before fever-chemotherapy. The daily urinary excretion of bismuth during the first 6 days remained consistently lower than 2 mg. A series of 8 patients received water-soluble bismuth intramuscularly in addition to the 2 cc. of oil-insoluble bismuth 16 hours before fever-chemotherapy. The urinary excretion of bismuth was above the therapeutic level during the 16 hours before fever-chemotherapy; however, during fever-chemotherapy and in the postfever period the excretion was less than the therapeutic level. Another group of 8 patients received 2 cc. of oil-insoluble bismuth 16 hours before treatment and water-soluble bismuth (38 mg. of elemental bismuth) 30 minutes before fever-chemotherapy. A therapeutic level was obtained during fever-chemotherapy the night after treatment, and the following 3 postfever days. In one of these cases, the patient developed acute nephrosis and ulcerative stomatitis. A series of 27 patients received a reduced dose of water-soluble bismuth equivalent to 19 mg. of elemental bismuth, and no serious reactions were noted. The urinary bismuth secretion was above the minimal therapeutic level during the fever-chemotherapy period, but less than this level during the following 5 postfever days. Among 26 patients receiving water-soluble bismuth containing 28.5 mg. of elemental bismuth 30 minutes before fever-chemotherapy, 1 patient developed acute nephrosis and stomatitis complicated with pneumonia and died 14 days after treatment.

Of a total of 69 patients who received water-soluble bismuth in addition to oil-insoluble bismuth, 10 had significant complications; of these, 3 were critically ill, and 1 died. Of an additional 173 patients given the same routine, except for the water-soluble bismuth, only 3 had complications and none were seriously ill.

The authors conclude that the addition of 19 to 38 mg. of elemental bismuth administered as a water-soluble compound to the fever-chemotherapy routine for early syphilis increases potential complications, and that the cotoxicities of bismuth, and arsenical compounds are additive when water-soluble bismuth in the doses mentioned is added.

A rapid and specific method for the estimation of bismuth in urine. Sidney Kaye and Julio C. Castillo. Am. J. Clin. Path., Baltimore, **8: 81, July 1944.**

The authors present a method for the estimation of bismuth in urine used in an Army laboratory for the routine analysis of urine of patients under antisyphilitic treatment. The essential features of the method are: (1) The deposition of the bismuth on a copper-wire spiral (Reinsch test) under controlled conditions. (2) Redissolving the deposited bismuth in dilute nitric acid in the presence of sodium sulfite. The interference of copper is eliminated by the addition of the sodium sulfite prior to redissolving the deposited bismuth in the dilute nitric acid. (3) Formation of bismuth-quinine-iodide and the nephelometric comparison of this with known bismuth standards.

The significance of the pH in the gold reaction. Carl Lange and Albert H.

Harris. J. Lab. & Clin. Med., St. Louis, 29: 970–975, Sept. 1944.

The satisfactory performance of tests that represent modifications of the original gold reaction requires an understanding of the effect of the pH of the milieu on the character of the curves. Strong buffers as diluents are desirable because they serve to maintain a uniform and correct pH. The optimal pH is 7.4, provided that an easily prepared citrate gold sol of constant and optimal sensitivity is used. An inadmissably low pH may easily be detected in unsatisfactory modifications of the gold reaction by the appearance of false paretic curves in purulent meningitis.

PUBLIC HEALTH ADMINISTRATION

Punishment for venereal disease in the Armed Forces ended by Congress. Editorial. J. A. M. A., Chicago, 126: 572, Oct. 28, 1944.

A public health step of first importance was taken when S. 1250 recently became law. The new measure abolished all punishment of members of the Armed Forces for the acquisition of venereal disease, provided only that the infected person complies with Army or Navy regulations requiring him to report and receive treatment. Failure to report a venereal disease infection remains punishable by court martial. Moreover, the measure provides that with exceptions noted, veterans who have acquired a venereal disease in line of duty are eligible for pension and compensation benefits if disability results.

The problem of syphilis as handled in the U. S. Navy. H. D. Newton. California & West. Med., San Francisco, 61: 149–150, Sept. 1944.

In spite of an intensive educational program constantly in effect, many man-days are lost in the Navy because of syphilis.

In one single Naval district the annual venereal disease rate was 25.57 per 1,000 men, and the syphilis-gonorrhea ratio was 1 : 13. Of 51 new cases of syphilis which came under the author's observation during the past year, 30 were seronegative primary syphilis and 21 seropositive primary syphilis. It is the author's opinion that because of educational programs and the frequent medical inspections a high percentage of the men report for treatment early in the course of the disease.

A standard practice is to follow up all cases of gonorrhea or chancroid with a Kahn test in 2 months. The screening of syphilitic patients under treatment to prevent assignment to duty where adequate treatment is not available is one of the important duties of a Naval medical officer. Regulation provides that a study of the physical condition, serologic reactions, and spinal fluid findings of men previously treated for syphilis is necessary before promotion from the enlisted personnel to a commissioned rank.

The procedure in false positive serologic reactions is to repeat the serologic tests in from 2 to 3 weeks, if malaria, catarrhal fever, one of the exanthems, or vaccination or immunizing injections have recently preceded the appearance of seropositivity and if there is no history or clinical evidence of the disease.

In a few instances in which reversal did not occur within a few weeks, spinal fluid studies revealed asymptomatic neurosyphilis.

The health needs of the nation as reflected by Selective Service. Leonard G. Rowntree. J. Michigan M. Soc., Lansing, 43: 769–777, Sept. 1944.

In an address before the 1943 Postgraduate Conference on War Medicine at the 78th Annual Session of the Michigan State Medical Society the author listed venereal disease among the four leading causes of rejections of registrants for military service.

Out of a total of 900,000 registrants found unfit for service with the Army (for the approximate period October 1940 until America's entrance into the war) because of physical or mental defects, 57,000 (6.3

percent) were rejected for venereal disease. In a second survey conducted through September 1941, venereal disease ranked seventh (5.9 percent) among the leading causes of rejections. Among white and Negro registrants, 18-19 years of age, for the period December 1942 to February 1943, syphilis was in second place among Negroes—112.0 rejections per 1,000. As of April and May 1943, syphilis accounted for more than 15 percent of the total rejections in the Negro group. For Negroes 20 years of age and over, syphilis was the leading cause of rejection (28.7 percent). Syphilis and tuberculosis, listed among the first 10 causes of rejections for Negroes, were lower on the list of causes for rejection in the white group.

As of April and May 1943, syphilis was in ninth place (4.4 percent).

Syphilis accounted for 301,400 (10.5 percent) and gonorrhea and other venereal diseases for 14,300 (0.5 percent) rejections among 2,870,000 registrants, 18-44 years of age, in class 4-F, as of April 30, 1943.

The author points out that for the first 2 years of the war, men with known venereal disease were not inducted. The rejection rate was high—contraction of venereal disease was one of the common methods of evading induction. Now, registrants with venereal disease have been inducted in increasing number.

Clinical, electrocardiographic and pathologic correlation of certain common cardiac conditions, and evaluation of the cardiac patient in industry. James M. Carlisle and Augustus Gibson. Indust. Med., Chicago, 13: 783–803, Oct. 1944.

Sudden death of persons with syphilitic heart disease occurs frequently enough to make this disease cause for rejection of such prospective employees. The diagnosis may be extremely difficult to make and requires the aid of fluoroscopic and roentgenographic examinations. Unless aortic insufficiency of long standing or coronary ostial stenosis is present, the electrocardiogram may not be abnormal. The former results in left ventricular hypertrophy and the electrocardiogram resembles that found in hypertensive heart disease. Coronary ostial stenosis may produce changes that are indistinguishable from those seen in arteriosclerotic heart disease.

An applicant for employment with positive blood serologic reactions having an aortic diastolic murmur or even an alteration in the character of the heart sounds in the aortic area should be rejected. By means of roentgenographic and fluoroscopic examinations, the examiner should look for hypertrophy of the left ventricle and signs of aortic dilatation. In searching for the latter, a simple A-P film is not sufficient. Lateral and oblique views and fluoroscopy are essential for the diagnosis.

The article is illustrated with color photographs of autopsy material, electrocardiograms, and roentgenograms.

A guide for the collection and mailing of specimens to the Virus Diagnostic Unit, State Division of Laboratories. California's Health, Sacramento, 2: 28–30, Aug. 31, 1944.

Lymphogranuloma venereum is included among the diseases for which routine diagnostic service is now offered by the California Division of Laboratories.

The complement fixation test is the type of examination preferred. Two blood specimens should be collected (10 cc.) aseptically in a sterile rubber-stoppered container and shipped by regular mail. Positive, doubtful, and negative results are reported and interpreted. The demonstration of rise in complement fixation titer in a second specimen over the first is of special significance in establishing a diagnosis, as a single positive result may indicate either current or past infection.

Containers for mailing specimens can be obtained from the Division of Laboratories, and the service is available to health officers, physicians, and hospitals.

Venereal disease contact investigation. Quart. Bull. Louisiana Dept. Health, New Orleans, 35: 5–6, June 1944.

During the first quarter of 1944, 3,686 persons were admitted to venereal disease clinics throughout the State, 2,432 (66 percent) being in the infectious stage. Of the

total new admissions, 2,618 had syphilis; 1,413 (54 percent) of these were infectious.

The new patients admitted to the clinics named 1,581 contacts, sexual and familial. The number of contacts with an infectious venereal disease was 0.5 per new admission. Fifty-seven percent of all contacts examined were found to be infected; contacts of patients with primary and secondary syphilis were infected in 71 percent of the cases, and of the contacts of patients with gonorrhea, 58 percent were infected.

On the basis that 57 percent of all contacts examined were infected, 1,200 persons with venereal disease were not located. A weakness in the venereal disease control program, is inadequate contact interviewing.

The Epidemiologic Index, which is the number of contacts examined divided by the number of new admissions times 100, shows the relative success of "shoeleather" epidemiology. An index number of 100 is desired, but 50 at present would be considered fairly good. The index number for all contacts is 20, with the highest index number (36) for contacts of primary and secondary syphilis. Another weakness in the control program is lack of success in getting named contacts examined.

At least one contact named and examined for each new admission should be the goal of every venereal disease clinic, or at least one contact named and examined for every new patient with early syphilis and/or gonorrhea. Until such a standard can be attained and maintained, effort should be made to locate and examine every named contact of patients with primary and secondary syphilis and gonorrhea.

Based on the figures presented, if the work had been confined to contacts of infectious patients with syphilis and gonorrhea, the number of infected persons located could have been increased at least 33 percent.

A sex education project and serologic survey in a Baltimore high school. C. Howe Eller. Baltimore Health News, 21: 81–88, Nov. 1944.

This project was conducted by the Johns Hopkins School of Hygiene and Public Health (syphilis study), in cooperation with the Baltimore Department of Education and the Baltimore City Health Department, among 903 white students, 371 boys and 532 girls, of the Patterson Park High School during April and May 1944.

A representative group of boys and one of girls was selected to assist in guiding the attitudes of the student body and report the results of the educational phase of the program. Forty-five minute talks were given during the regular health education periods; this allowed separation of the sexes without undue accentuation. The talks included: (1) A discussion with illustration of the anatomy and physiology of the male and female reproductive systems, omitting detailed discussion of intercourse and childbirth; (2) an outline of reasons for judgment in sex practice (religion, morals, ethics, social and economic dependency), and (3) brief descriptions of the etiology, diagnosis, and treatment of venereal disease.

In subsequent meetings with the 2 leader groups, it was found that the boys were less expressive than the girls. The boys felt that the venereal disease educational program should be a permanent part of the high school curriculum. The girls stated that the pamphlet "Growing Up in the World Today," distributed during the lectures, furnished a basis for discussion with parents.

Of the 903 pupils, 726 (80.4 percent) had their parents' consent to submit to the serologic test for syphilis, 103 refused the test, and 74 made no reply. No case of syphilis was found among the 726 students.

Venereal disease education. Association Notes. Mil. Surgeon, Washington, 95: 246, Sept. 1944.

The U. S. Public Health Service Advisory Committee on Public Venereal Disease Education has submitted to the Surgeon General a report of a special meeting at which representatives of 47 religious, social service, health welfare, and other similar organizations expressed opinions on questions concerning public venereal disease education.

The report included the following recom-

mendations: (1) That the Surgeon General not sponsor the exhibiting in commercial picture houses the film "To the People of the United States," and that the film be revised for use by selected noncommercial groups. (2) That several existing films be revised slightly and used more extensively. (3) That promiscuity be dealt with in venereal disease control educational activities. (4) That radio is an acceptable means of disseminating information to the public. (5) That the showing of motion pictures to selected groups must be utilized extensively. (6) That commercial motion pictures should be utilized to the greatest extent practicable through programs maintaining high standards. (7) That films intended for general motion picture audiences should provide strength in presentation of moral and ethical values, condemnation of promiscuity, dramatic value, good technical work, and avoidance of indecent incidents. (8) That the subject matter of commercial films be stated in advance by reviews, advertisements, and appropriate notices that the program includes the subject of venereal diseases. (9) That collaboration with volunteer agencies and the U. S. Public Health Service be effected through conferences at regular intervals.

Contact investigation in gonorrhea. Nobel W. Guthrie. Am. J. Syph., Gonor. & Ven. Dis., St. Louis, 28: 571–582, Sept. 1944.

Data are compiled of the investigation of contacts of gonorrhea patients admitted to the Venereal Disease Division of the Johns Hopkins Hospital from Aug. 1, 1942 through May 30, 1943. This study is an attempt to measure results of tracing contacts of gonorrhea.

It was found that male patients gave more contact information leading to discovery of a new infection than did female patients (38 new infections found per 100 male original patients, as compared with 16 per 100 female patients).

In following local sexual contacts of adult original patients, a higher proportion of infected contacts was found among females. The two factors involved were (1) a higher proportion of named female contacts (0.75) was examined than male (0.62), and (2) of those examined, a higher proportion of female patients (0.61) had new gonorrhea than of male (0.19). The combined effect of these two factors is expressed by the proportion of named contacts examined and found to have new gonorrhea (0.46 female; 0.12 male). During the period in which these data were collected, the investigation of a local female sexual contact of an adult original patient was 3.8 times more likely to lead to discovery of a new gonococcic infection than was investigation of a male contact of a similar type.

The cost in visits per new infection found as a result of contact visiting was 23 for male contacts and 3.6 for female contacts.

Repeated examinations of contacts were less productive than initial examinations.

The author outlines what he believes to be a reasonable compromise between effectiveness and economy in investigating gonorrhea contacts. In interviewing adult patients, data should be secured on contacts exposed sexually during the 2 weeks prior to onset, or since onset, in male patients, and during the month preceding the interview in female patients. In following contacts of adult male patients, administrative effort only should be used. In the case of female patients, administrative effort should be made first. If the contact is not examined during the week following the interview, one visit should be made. If the contact does not respond to the visit, investigation may be dropped or further administrative effort tried. More than one visit to a contact should not be made except under exceptional circumstances. Administrative efforts but not visits may be used to secure additional examinations of contacts whose first examination was negative.

Syphilis in gonorrhea patients and contacts. Nobel W. Guthrie. Am. J. Syph., Gonor. & Ven. Dis., St. Louis, 28: 583–587, Sept. 1944.

Gonorrhea patients and contacts in-

cluded in a previous report (page 571 of this journal) were studied regarding the prevalence and incidence of syphilis. Negro patients were found to have syphilis three times as frequently (35 percent) as white patients (13 percent), and Negro female patients more often (44 percent) than Negro male patients (26 percent). Of 396 patients admitted to the Johns Hopkins Hospital, 31.3 percent had syphilis on admission, and of 205 contacts examined, 39 percent had syphilis on admission.

The age–specific syphilis rates in Negroes rose from about 5 percent in the group under 10 years of age to 50 percent in the 30–39–year–age group.

One hundred and twenty-eight nonsyphilitic gonorrhea patients were reexamined for syphilis during the 12 weeks following admission. They accumulated 840 person-weeks of observation, and 3 were observed to have developed syphilis. This relatively low rate at which gonorrhea patients develop syphilis does not justify frequent blood testing. Patients may be inspected for lesions when the necessary observations for gonorrhea are made. Serologic tests for syphilis should be made on admission and at 4- or 6-week intervals during the next 12 weeks.

Workmen's Compensation Acts: Cerebral hemorrhage following exertion in hot weather by syphilitic workman. J. A. M. A., Chicago, **126: 126, Sept. 9, 1944.**

The workman, a Negro about 40 years of age, had syphilis in the tertiary stage, and the court stated that he enjoyed good health prior to the date of the industrial accident. While unloading lumber from boxcars on a very warm day, the workman became overheated and dizzy but continued working another hour until the day's work was finished. He was sick at night, and when attempting to begin work in the morning he became unconscious. Subsequently, he had a cerebral hemorrhage which resulted in paralysis of his left side. He was denied compensation under the Florida Workmen's Compensation Act and also by the circuit court. He then appealed to the Supreme Court of Florida.

The Supreme Court concluded that the workman was entitled to compensation on the theory that the exertion of his employment had accelerated or aggravated his syphilitic condition. Recovery of compensation by a claimant is not conditioned on good or perfect health. The employer accepts the workman in such physical condition as he finds him and assumes the risk of a disease condition aggravated by injury. Compensation is not made on the condition of health of the workman but on an injury which is a hazard of employment.

Erratum

The article entitled "Prevalence of Gonorrhea Among Syphilitic Patients: A Study Made in Delaware in 1943," by A. R. Cameron and A. L. Chapman, which appeared in the August 1944 issue of this journal contained two errors. In table 6, page 239, the number of cases having no recurrences should have appeared as 112 instead of 110. Also on page 240 the first line should read: "In 257 or 70 percent of these patients" instead of "In 391 or 94 percent of these patients."

New Cases of Syphilis and Gonorrhea in States, Territories, and Possessions

Health officers' monthly statement: Reported for the first 3 months of fiscal years 1944–45 and 1943–44

Area	Cases of syphilis and gonorrhea reported for first 3 months of fiscal years below:											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944–45	1943–44	1944–45	1943–44	1944–45	1943–44	1944–45	1943–44	1944–45	1943–44	1944–45	1943–44
Total † United States..	[1]86,951	[1]120,211	[1]18,356	[1]19,465	[1]23,680	[1]32,596	[1]35,338	[1]51,947	[1]2,956	[1]3,483	[1]73,251	[1]75,458
Alabama.....	3,774	4,305	534	612	776	976	708	1,095	62	120	1,674	1,882
Arizona.....	(*)	800	(*)	179	(*)	220	(*)	314	(*)	32	(*)	483
Arkansas.....	2,125	2,338	406	325	687	829	810	830	68	61	1,325	1,206
California.....	7,522	8,459	1,385	1,300	1,680	1,979	4,108	4,732	236	261	9,716	7,753
Colorado.....	642	1,125	178	258	201	310	239	509	24	48	651	766
Connecticut....	676	791	67	91	344	272	113	252	18	48	318	368
Delaware.....	198	265	43	23	56	61	82	32	7	4	76	49
Dist. Columbia.	238	1,975	32	260	52	479	107	1,124	8	37	227	842
Florida.....	3,651	8,596	594	806	1,194	2,597	1,496	3,959	88	183	3,862	4,769
Georgia.....	2,860	5,030	738	929	1,153	2,081	865	1,863	104	155	1,806	3,032
Idaho.....	272	109	58	66	62	19	144	20	6	1	165	172
Illinois.....	5,615	7,527	921	913	1,305	1,877	3,208	4,578	181	159	5,644	6,555
Indiana.....	1,502	2,141	338	302	197	202	504	820	54	70	1,004	908
Iowa.....	398	640	85	138	101	169	169	267	25	48	662	493
Kansas.....	684	682	161	111	123	138	364	409	36	24	750	576
Kentucky.....	1,374	2,088	321	246	324	450	528	896	76	79	1,232	942
Louisiana.....	3,536	4,879	802	757	1,075	1,348	850	1,538	134	128	4,199	3,382
Maine.....	252	217	58	46	27	26	89	111	22	18	578	318
Maryland.....	2,244	4,492	473	417	566	458	560	642	45	32	1,275	2,207
Massachusetts..	1,059	1,263	271	284	(§)	(§)	721	924	67	55	1,192	1,159
Michigan.....	4,555	4,680	723	619	1,284	1,153	1,692	1,984	131	132	3,119	2,927
Minnesota.....	557	660	92	69	55	77	368	460	25	41	632	557
Mississippi.....	5,568	6,844	1,852	2,261	1,566	2,034	1,807	2,247	343	302	8,400	7,757
Missouri.....	2,370	2,337	551	425	622	590	1,024	1,064	81	91	1,993	1,269
Montana.....	124	108	32	33	16	11	36	48	3	3	83	114
Nebraska.....	329	321	52	57	81	188	184	51	9	12	543	475
Nevada.....	132	187	40	1	1	38	52	137	5	9	152	108
New Hampshire	72	41	4	8	4	21	55	9	7	0	44	39
New Jersey....	2,076	2,878	351	356	535	921	1,090	1,501	77	98	1,462	1,486
New Mexico...	395	520	93	108	105	131	176	245	35	36	362	364
New York.....	7,011	10,017	1,416	1,447	1,364	1,764	3,968	6,425	178	275	3,594	5,116
North Carolina.	2,274	3,010	903	745	834	1,174	495	1,032	42	59	2,917	2,497
North Dakota..	62	74	12	20	7	13	26	30	4	3	109	79
Ohio.....	4,700	6,323	975	822	1,325	1,451	2,218	3,080	182	189	2,135	1,300
Oklahoma.....	(*)	2,192	(*)	290	(*)	648	(*)	808	(*)	92	(*)	1,313
Oregon.....	537	596	118	152	63	45	310	392	30	7	588	567
Pennsylvania...	2,964	3,515	534	449	890	1,475	1,000	1,272	85	169	0	303
Rhode Island...	235	289	76	21	19	26	105	212	8	4	627	213
South Carolina.	2,358	4,680	598	968	743	2,021	836	1,487	68	125	1,817	1,618
South Dakota..	100	138	15	24	35	21	36	61	14	11	129	117
Tennessee.....	4,051	4,695	600	698	1,587	1,924	1,588	1,891	114	108	3,284	4,207
Texas.....	4,229	5,984	851	801	1,468	1,681	1,500	2,199	161	146	2,601	2,638
Utah.....	160	257	45	58	8	35	105	158	2	6	183	176
Vermont.....	42	64	6	20	9	16	22	26	4	2	126	47
Virginia.....	2,396	3,730	741	1,217	934	1,337	646	1,022	56	89	1,306	3,359
Washington....	(*)	1,037	(*)	186	(*)	256	(*)	423	(*)	26	(*)	2,094
West Virginia..	560	1,152	148	164	64	146	89	216	10	28	644	670
Wisconsin.....	(*)	288	(*)	53	(*)	0	(*)	233	(*)	2	(*)	368
Wyoming.....	472	189	63	38	138	32	245	97	21	7	45	76
Territories, Possessions, and Panama C. Z.												
Alaska.....	28	23	8	12	4	4	7	3	1	1	166	93
Canal Zone....	299	(*)	40	(*)	57	(*)	165	(*)	13	(*)	138	(*)
Hawaii.....	243	240	89	51	29	26	111	148	10	14	560	403
Puerto Rico....	3,328	6,092	524	551	1,095	1,282	1,009	1,830	659	720	1,732	1,045
Virgin Islands..	68	60	8	14	46	34	7	9	2	3	27	57
Actual total ‡ U. S. Territories and Possessions.	90,917	130,943	19,025	20,801	24,911	35,066	36,637	55,715	3,641	4,373	75,874	81,314

* No data available.

** Includes "not stated".

† Based on States reporting in both fiscal periods.

‡ Includes all reported cases.

§ Included in late latent.

[1] Based on 44 States and the District of Columbia.

New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over

Health officers' monthly statement: Reported for the first 3 months of fiscal years 1944–45 and 1943–44

City	Cases of syphilis and gonorrhea reported for first 3 months of fiscal years below:											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44
Total †	[1]25,765	[1]35,924	[2]5,298	[2]4,199	[2]5,803	[2]7,909	[2]11,174	[2]16,748	[2]625	[2]761	[1]17,829	[1]15,448
Akron	237	266	60	28	50	68	109	158	18	12	181	110
Atlanta	656	864	190	185	187	263	268	405	11	11	849	298
Baltimore	1,465	3,636	403	315	364	296	470	483	16	15	707	911
Birmingham	823	1,405	90	88	216	360	196	348	20	26	140	137
Boston	384	470	81	107	80	0	186	284	18	9	409	330
Buffalo	(*)	435	(*)	50	(*)	78	(*)	296	(*)	11	(*)	210
Chicago	(*)	3,830	(*)	600	(*)	997	(*)	2,145	(*)	88	(*)	3,567
Cincinnati	594	806	103	114	(§)	(§)	491	692	(§)	(§)	284	281
Cleveland	1,157	1,042	229	167	397	353	506	493	25	29	484	341
Columbus	348	389	105	64	84	78	149	234	10	13	134	99
Dallas	(*)	648	(*)	128	(*)	126	(*)	388	(*)	6	(*)	196
Dayton	276	510	35	50	88	150	141	288	12	22	159	149
Denver	273	575	76	97	94	137	87	221	6	16	235	439
Detroit	2,673	3,127	497	351	912	944	1,206	1,772	58	60	1,574	1,421
Honolulu	66	148	21	29	8	19	34	90	2	10	296	287
Houston	441	495	99	81	161	175	162	219	19	20	534	608
Indianapolis	469	593	103	211	59	4	121	127	6	6	140	34
Jersey City	103	148	10	17	31	34	56	98	6	9	19	13
Kansas City	379	456	79	73	81	65	193	292	18	24	260	242
Los Angeles	2,866	2,932	805	0	399	1,105	1,571	1,738	91	89	1,749	1,215
Louisville	280	708	81	80	58	120	115	273	14	6	327	236
Memphis	(*)	1,777	(*)	155	(*)	849	(*)	752	(*)	21	(*)	1,574
Milwaukee	109	127	22	14	0	0	85	99	2	1	126	73
Minneapolis	158	196	46	36	25	35	83	119	4	5	270	239
Newark	433	575	95	75	134	144	197	345	7	11	314	244
New Orleans	442	618	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	536	262
New York	4,883	6,975	1,164	1,136	1,176	1,566	2,360	4,039	119	170	3,594	3,581
Oakland	390	445	50	49	90	109	212	277	7	7	444	346
Oklahoma City	(*)	449	(*)	58	(*)	154	(*)	188	(*)	10	(*)	237
Omaha	128	141	18	10	21	98	84	23	5	10	116	143
Philadelphia	1,484	2,074	193	121	249	493	310	521	28	47	240	169
Pittsburgh	(*)	2,171	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)
Portland	231	292	71	67	32	19	125	206	3	0	419	237
Providence	106	140	14	11	11	6	60	113	3	2	28	44
Rochester	71	62	16	13	4	3	50	44	1	2	105	68
St. Louis	1,468	1,356	320	195	442	476	659	635	47	40	1,008	373
St. Paul	57	78	12	12	13	17	24	39	2	3	60	95
San Antonio	296	330	25	38	67	84	155	194	10	14	265	332
San Diego	399	271	46	16	110	71	197	174	19	10	336	185
San Francisco	745	845	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	677	537
Seattle	345	352	82	38	79	70	174	216	3	7	419	419
Syracuse	149	231	9	6	8	10	130	203	2	12	114	79
Toledo	143	271	16	45	21	58	101	162	5	6	50	29
Wash'n, D. C.	238	1,975	32	260	52	479	107	1,124	8	37	227	842
Actual total ‡	25,765	45,234	5,298	5,190	5,803	10,113	11,174	20,517	625	897	17,829	21,232

* Data not available.
** Includes "not etated."
† Based on cities reporting in both fiscal periods.
‡ Includes all reported cases.
§ Included in late latent.

[1] Based on 38 cities.
[2] Based on 36 cities.

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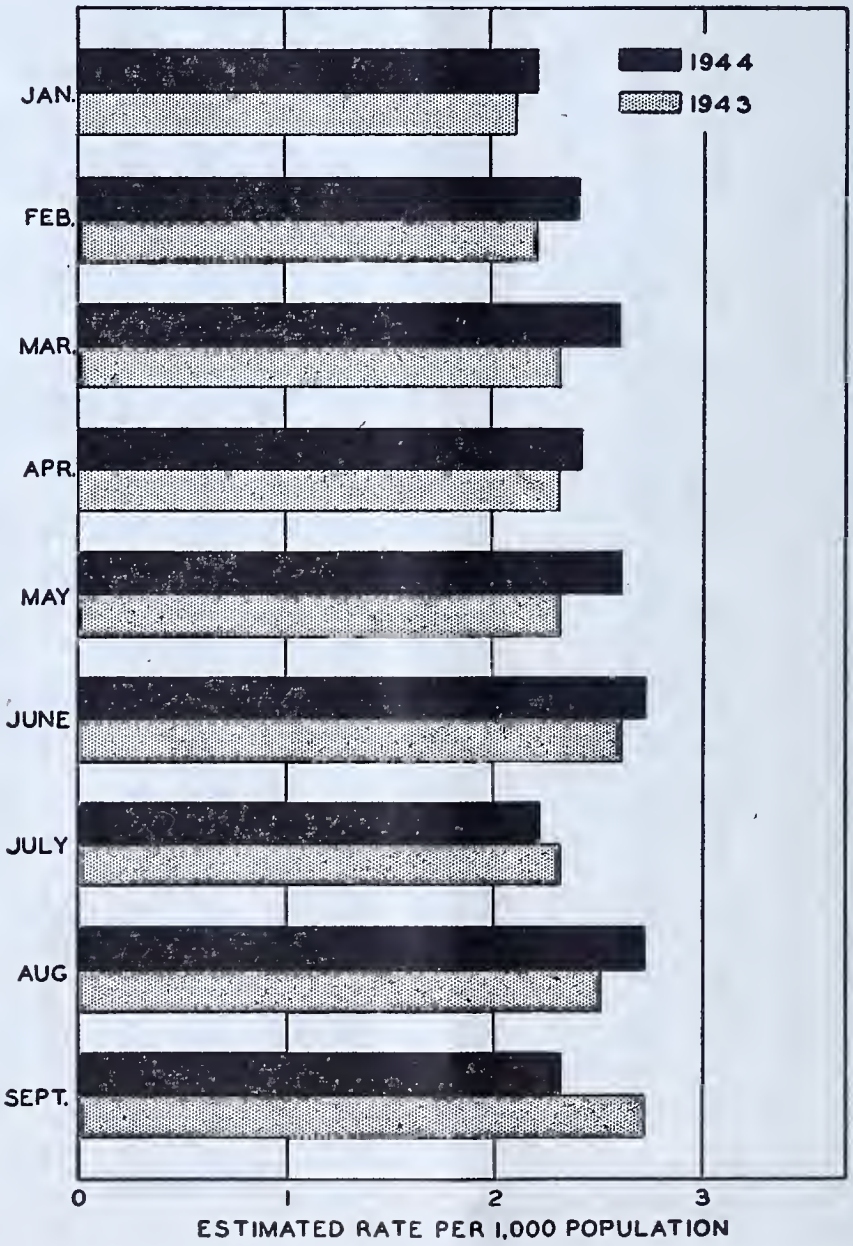
ANNUAL GONORRHEA CASE RATES IN THE UNITED STATES
BASED ON PROVISIONAL MONTHLY DATA 1944 AND 1943



Venereal Disease Information

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FEDERAL SECURITY AGENCY

UNITED STATES PUBLIC HEALTH SERVICE

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The Medical Officer and the Venereal Disease Education of the Soldier

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Education, an important factor in the control of venereal diseases in civilian life, is the most significant part of the program in the Army. In civil communities sound control efforts are based primarily on epidemiology, and the responsibility for control of the sources of venereal disease infection is shared jointly by civil health and law enforcement agencies. Because the U. S. Army has no authority to deal with the sources of infection of military personnel, it must depend on civilian cooperation for such assistance, and within itself, it must rely primarily on education. True, the Army may, by restrictive action, prevent access of its personnel to certain undesirable elements of the civil population but such action is of narrow application and limited usefulness. Our most practical weapon is education—education to avoid exposure, education to use prophylaxis, education to seek early treatment from military medical sources if the first two admonitions are not heeded.

The importance of venereal disease education is officially recognized in the U. S. Army by regulation and directive. Unfortunately, these provisions have been considered by many as the maximum educational requirements rather than as a minimum acceptable standard. Regardless of the interpretation of official directives, the fact that most of our current infections occur in personnel who are ignorant of venereal disease facts indicates either that we have failed to appreciate the importance of education, or that we have neglected to utilize available technics and to develop new procedures. Syphilis and gonorrhea are preventable diseases.

The basic principles of a sound venereal disease educational policy are the following:

1. Venereal disease education must be properly motivated.
2. Venereal disease education must be adapted to the personnel to be trained.
3. A few scientifically accurate facts must be presented with a well defined purpose.
4. The presentation must be well organized, coordinated, progressive and repetitive, but at the same time, simple, brief and attractive.

The proper method of motivation of venereal disease education is not only frequently misunderstood, but often is completely ignored. In presenting the reasons for giving instruction concerning venereal disease, it is well to recall that the sex habit pattern of many men is probably well established by the time they reach the Army, and there is little reason to believe we can alter their behavior. We must also recognize the fact that at times passion may outweigh judgment, and we must provide convincing justification—not for the lapse of self-control, but for the use of prophylaxis. It is of no avail to expose even the most intelligent of these individuals to carefully selected information, desirably presented, if he will not use it. The soldier must be moved to utilize the information imparted. That can be done by motivation. Our appeal must be so fortified that it will surmount the "it can't happen here" complex.

All soldiers are susceptible to the appeal to personal and organizational pride in remaining free from infection in order to contribute their individual share of service to a more efficient organization. Such an approach can be closely associated with patriotism. Even the most calloused individual hates to be called a poor soldier. The fact that venereal disease infection

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terial must follow an exact plan, each step accomplished by selected material and contributing to a definite purpose. That program should be a part of the general military training program. It must be coordinated with other phases of training, in order that the educational process does not become boring through repetition of old ideas by too familiar technics, that the stimuli will be strongest when most needed, and that learning progresses from simple facts to more complicated information. Through this entire process, the original basic principles must be reiterated: that venereal disease is preventable through continence and by prophylaxis, and that if reason gives way to emotion, then common sense must assert itself.

Venereal disease education is like some forms of immunization. The original dose should build up a high protective level, but periodic stimulation will be necessary to maintain that level and to insure adequate protection at moments of particular stress. In the initial presentation, the salient facts are presented with their justification—ordinarily by motion pictures and a discussion. The stimulating dosages can consist of such devices as properly placed posters, a stamp on the back of passes illustrating the location of "green light stations," a "throw-away" sheet on payday, or a reminder from the sergeant to the soldier before his departure for furlough that the Army has a stake in his health. When it becomes desirable to raise the general "immunizing educational level," new material should be introduced—a different film, a fresh approach to the entire problem. On such occasions it is effective to *see* a film, *hear* a brief supplementary explanation and *read* a pamphlet, which will summarize and perhaps augment the arguments, having the final effect of a delayed reinforcement of the previous efforts. This use of a unit of material consisting of a film, a pamphlet, and a discussion has been very popular. It demands considerable educational material, but this can often be prepared locally. Aside from motion pictures, training aids developed on a local level are the most effective, for they are adapted to specific problems and interests, and in themselves stimulate a desirable consideration of the subject.

Such a program as here suggested need not be time consuming, when established as part of a general training routine of which it is rightly an integral unit. The supervision is a duty of the medical officer, but its conduct should not be his responsibility alone. Medical officers, chaplains, and special service (morale) officers have their particular roles, but none compares in importance with that of the unit commander. No other single educational device is as effective as a reminder from the man to whom troops look for leadership. A simple statement, a compliment on a good record long-maintained, or a warning if a lapse from creditable behavior occurs, by the unit commander is worth far more than hours of haranguing by medical officers. The mere recognition of venereal disease prevention is in itself a stimulant to control measures.

Such participation cannot be gained, or more important still, command support for the entire venereal disease control program cannot be expected unless officers are properly educated. They cannot teach if they are not informed, though such information need not be technical. Officer education is not ordinarily considered as part of the venereal disease education of the soldier, yet it is the foundation of that program. Its importance cannot be overestimated. On the local level, officer training is best effected by an informal, personal interview with the officer concerned, with a frank exposition of the purpose of the proposed educational program, constantly emphasizing the importance of such activities as a preventive measure—dividends to be paid in better health, improved morale, more training and increased efficiency. In the higher echelons, command support must be acquired by definition of a sane administrative policy relative to the venereal diseases, by a careful exposition of the problem, a concise statement of the purposes of an educational program and the results to be anticipated.

No detailed account can be taken here of certain specialized features which are part of a broad venereal disease educa-

tional program. Such items include the teaching of inductees, instructions of female personnel, special information regarding the venereal disease problem in theaters of operation for troops about to embark, instruction of men already infected, the important aspects of professional education, and the indoctrination of officer candidates and students in specialty schools. For those in a supervisory or consultative capacity professional education is of extreme importance. The education of particular groups with specially difficult problems is a challenge to the ingenuity. In many of the Negro organizations of the Army Air Forces, an intensive educational program for noncommissioned officers has been conducted, resulting in spectacular achievements in some organizations. This program has embodied the principle previously described, extending command responsibility into the lowest echelons, and emphasizing the importance of self-participation, and group and racial pride.

There is much more than has been mentioned here which can be accomplished in the field of venereal disease education, particularly in relation to contributions to the health knowledge of the civilian community. To you for whom civil and military health administration is related so closely, this has special implications. When peace comes, the venereal disease knowledge gained in service by the millions of men released from the Army and Navy will make a considerable impression upon community health programs; but at present we are concentrating on winning a war, and any deflection from our contributions to that objective is unthinkable. The effectiveness of our educational endeavors in helping to prevent and curtail the disability from venereal disease in the Army will be greatest if we do not forget:

1. Venereal disease education must be properly motivated.
2. It must be adapted to the personnel to be treated.
3. A few scientifically accurate facts must be presented with a well defined purpose.
4. The presentation must be well organized, coordinated, progressive and repetitive, but at the same time, simple, brief and attractive.

Penicillin Serum Concentrations in the Treatment of Gonorrhea by Delayed Intramuscular Absorption

B. L. Zinnamon, Passed Assistant Surgeon (R)[1] and V. P. Seeberg, Ph.D.[2]

A method of delaying intramuscular absorption of penicillin using a beeswax and peanut oil suspension was recently reported by Romansky and Rittman (*1*). Because of difficulties in adjusting penicillin treatment schedules for venereal disease patients to clinic or office practice using saline solution as a diluent, we have also been interested in this problem for some time, and have obtained varying degrees of retardation by combining penicillin[3] with aluminum hydroxide, pectin, globin, and various fixed oils (unpublished data). Using these combinations experimentally in rabbits, the most pronounced slowing of absorption was found with a sesame oil or peanut oil suspension, either of which maintained assayable serum levels approximately 50 percent longer than the same quantity of penicillin administered in physiologic saline solution.

Following the publication of the work by Romansky and Rittman we confirmed the further delaying effect of the addition of beeswax to the oil suspensions. This, in our opinion, brought the problem to a

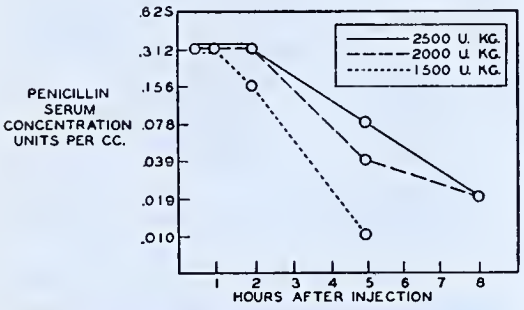
[1]U. S. Public Health Service; also Venereal Disease Consultant, Oakland City Health Department, Oakland, Calif.

[2]Pharmacologist, Cutter Laboratories.

[3]The sodium penicillin used was purchased through official depot hospitals and represented the products of several different manufacturers. The calcium penicillin was furnished by Cutter Laboratories from material allocated by W. P. B. for clinical evaluation studies.

point where a definite practical advantage could be derived from the use of the delayed absorption technic in our clinic patients.

In order to approximate the dosage required to attain and maintain effective therapeutic serum levels with the penicillin–beeswax–oil suspensions in human beings, rabbits were injected with 1,500, 2,000, and 2,500 units of penicillin per kilogram body weight and serum levels were followed at intervals during an 8-hour period. On this basis a human dosage of 150,000 units was arbitrarily selected as one which might give effective therapeutic levels for approximately 8 hours.



Penicillin serum concentrations in rabbits injected with various doses of penicillin in 1 percent beeswax in sesame oil

Difficulty was encountered in obtaining a uniform suspension of the penicillin in the oil–wax mixture in the standard vial of dry penicillin by shaking with glass beads as described by Romansky and Rittman. Also a considerable loss of penicillin occurred because of a large portion of the comparatively small total volume of the oil suspension adhering to the sides of the vial. A more uniform suspension was obtained and less penicillin was lost by preparing the suspension under sterile conditions in a small mortar. Using this method, more satisfactory preparations were obtained with the calcium salt than with the sodium salt because of the hygroscopic properties of the latter, and a tendency to lump when exposed to air.

The volume of suspension injected was kept constant at 3 cc. of the oil-wax mixture per patient, 150,000 units of penicillin (averaging about 250 mg.) being readily suspended in this amount of liquid. Satisfactory suspension of this quantity of penicillin may also be made with smaller volumes of the oil-wax mixture. However, in preliminary experiments we found no significant differences in the height of or duration of the serum concentrations by varying the injected volume from 2 to 5 cc.

For the clinical studies we chose the sesame oil rather than the peanut oil as we felt it to be somewhat less allergenic. The beeswax used was U.S.P. white wax.

Twenty-nine patients were chosen from the female gonorrhea clinic of the Oakland Health Department for treatment.[4] Twenty-five were treated with the penicillin–oil–beeswax suspension consisting of 150,000 units of calcium or sodium penicillin in sesame oil with 1 or 2 percent beeswax and 4 were treated with 150,000 units of penicillin in physiologic saline to serve as controls. The total dosage for all patients was administered in a single intramuscular injection. All of the cases were of the routine type found in any venereal disease clinic and there was no selection of cases excepting that none of the patients were then currently being treated for their infection (treatment resistant cases). Diagnosis and follow-up studies were made by combined urethral and cervical cultures in the clinic laboratory. All patients were given their single injection of drug at 9 o'clock in the morning and required to remain in the clinic during the next 8 hours. Sterile blood specimens were drawn at varying intervals during the ensuing 8-hour period. All of the specimens were held overnight at about 4°C. and the penicillin serum concentrations determined the next day according to the method of Rammelkamp (*2*). The studies were carried out with groups of no more than 3 to 4 patients on a single day. Because of the difficulties encountered in case holding in the class of patients being treated, it is routine in our clinic to perform follow-up examinations and cultures at weekly intervals following treatment for a total of 3 consecutive examinations. If the patients remain negative at the end of this period of ob-

[4]These facilities as well as the laboratory facilities were made available for our use through the courtesy of Dr. S. F. Farnsworth, Health Officer, Oakland Health Department.

Serum penicillin concentration and culture data on patients treated with a single intramuscular injection of 150,000 units of penicillin

Patient number	Vehicle	Salt	Time period after injection							
			1 hr.	2 hr.	4 hr.	6 hr.	8 hr.	1 wk.	2 wk.	3 wk.
			Serum penicillin concentration, units per cc.					*Culture results*		
1	1% wax–oil	Sod.	--------	0.156	0.156	0.078	0.019	(1)	--------	--------
2			--------	0.156	0.156	0.039	0.019	Neg.	Neg.	Neg.
3			--------	0.156	0.039	0.019	0.007	Neg.	Neg.	Pos.[2]
4		Cal.	--------	0.625	0.156	0.078	0.019	Neg.	Neg.	Neg.
5			--------	1.250	0.625	0.078	0.019	Neg.	Neg.	Neg.
6			--------	0.156	0.312	0.078	0.039	Neg.	Pos.[2]	--------
7			--------	0.312	0.078	0.019	0.019	Pos.[3]	--------	--------
8			--------	1.250	0.078	0.019	0.007	Neg.	Neg.	Neg.
9			--------	1.250	0.156	0.078	0.019	Neg.	Neg.	Neg.
10			--------	0.625	0.078	0.019	0.007	Neg.	Neg.	Neg.
11			--------	1.250	0.078	0.019	0.007	Neg.	Neg.	Neg.
12	2% wax–oil	Sod.	--------	--------	--------	0.078	0.019	Neg.	Neg.	Neg.
13			--------	--------	--------	0.078	0.019	Neg.	Neg.	Neg.
14			--------	--------	--------	0.019	0.007	Neg.	Neg.	Neg.
15			--------	--------	--------	0.019	0.019	Neg.	Neg.	Neg.
16			--------	--------	--------	0.039	0.019	Neg.	(1)	--------
17			--------	--------	--------	0.078	0.019	(1)	--------	--------
18		Cal.	--------	0.624	--------	0.039	0.019	Neg.	Neg.	Neg.
19			--------	0.156	--------	0.078	0.019	Neg.	Neg.	Neg.
20			--------	0.312	--------	0.039	0.039	Neg.	Neg.	Neg.
21			--------	0.156	--------	0.039	0.019	Neg.	Neg.	Neg.
22			--------	0.312	0.312	0.156	0.039	Neg.	(1)	--------
23			0.312	0.156	--------	0.078	0.039	Neg.	Neg.	Pos.[2]
24			0.312	0.312	0.156	0.039	0.019	Neg.	Neg.	Neg.
25			0.312	0.625	0.312	0.078	0.039	Neg.	Neg.	Neg.
26	Saline	Sod.	0.312	0.156	0.019	Neg.	Neg.	Neg.	Neg.	Neg.
27			Not assayed					Pos.[3]	--------	--------
28			0.625	0.078	0.007	Neg.	Neg.	Neg.	Neg.	Pos.[3]
29			1.250	0.078	0.007	Neg.	Neg.	Neg.	Neg.	Neg.

(1) Left town.
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servation they are discharged as probably cured. (It is not our intention to establish this method of follow-up as the criteria of cure.) Nineteen of the patients treated were of the white race and 10 were Negroes.

The table shows the serum values as well as the results of the laboratory follow-up on all of the patients studied.

Of the 4 patients treated with the saline solution of penicillin, 1 was not assayed because of bacterial contamination in the blood samples. The other 3 showed demonstrable serum concentrations up to a 4-hour period only. All of the patients treated with the penicillin–oil–wax suspensions had demonstrable serum concentrations at the end of the 8-hour period.

No particular differences were noted in the serum levels obtained with the calcium or sodium salts. The 1 percent oil–wax suspension gave somewhat higher serum level peaks following injection than the 2 percent; the 1 percent suspension showed levels of 1.25 units per cc. 4 times out of 11 at the 2-hour period while none of the 2 percent suspensions gave this concentration. However, the 2 percent oil–wax suspensions in general showed somewhat higher levels at the end of the 8-hour period, the serums assaying 0.039 units per cc. 4 times in 14 patients while the 1 percent oil–wax suspension assayed at this level only once in 11 patients. There was no complaint of pain at the site of injection by any of the patients at the time of administration or during the posttreatment period, other than the transitory reaction following any intramuscular injection. No systemic reactions of any type were observed.

Unfortunately, the series of cases studied was too small and the particular group of patients treated too uncooperative for us to draw any definite conclusions as to the

point where a definite practical advantage could be derived from the use of the delayed absorption technic in our clinic patients.

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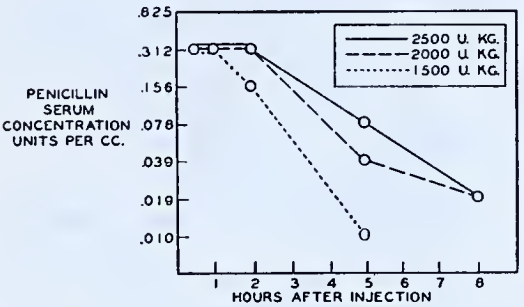

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Unfortunately, the series of cases studied was too small and the particular group of patients treated too uncooperative for us to draw any definite conclusions as to the

value of this treatment as compared to current treatment methods. Of the 4 patients treated with the saline solution of penicillin, 2 remained negative throughout the period of observation, while 2 developed positive cultures, 1 on her first reexamination and 1 on her third. Of the 25 patients treated with the penicillin–oil–wax mixture, 4 left town during their follow-up period, 2 following their first examinations, (both negative) and 2 without any follow-up examinations. Of the remaining 21 patients, 4 had positive cultures during their follow-up examinations. However, 3 of the patients admitted having intercourse, in each instance naming their original source of infection as their contact. Two of these contacts were examined in the clinic and found to have positive urethal and prostatic cultures. The third contact was under treatment in the clinic at the time of exposure and was known to be positive. These 3 patients have been classified as reinfections rather than treatment failures. The fourth patient we feel is a definite treatment failure. Excluding those patients who did not follow through with their posttreatment examinations and the 3 patients classified as reinfections, we can report 1 definite treatment failure out of 18 patients followed through the 3-week observation period.

CONCLUSIONS

1. Varying degrees of retardation of intramuscular absorption of penicillin were obtained by combining the substance with aluminum hydroxide, pectin, globin and various fixed oils. Of these, the fixed oils effected the most retardation, increasing the duration of assayable serum concentrations with a given dose by about 50 percent over a penicillin-saline solution.

2. The further delaying effect of the addition of beeswax to the oil suspensions as proposed by Romansky and Rittman has been confirmed.

3. Favorable therapeutic serum concentrations were maintained for 8 hours in 25 patients after a single intramuscular injection of 150,000 units of penicillin suspended in a beeswax and sesame oil mixture.

4. Slightly more delaying effect was noted with a 2 percent wax suspension than a 1 percent. No particular difference in serum levels between sodium and calcium salts was noted. Calcium salts gave more satisfactory suspensions.

5. Seventeen female patients with acute gonorrhea out of 18 treated and successfully followed were rendered negative for a 3-week posttreatment period by a single intramuscular injection of penicillin in beeswax and sesame oil. Two patients out of 4 treated with the same quantity of penicillin in physiologic saline were rendered negative for the same period.

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DIAGNOSIS

Abdominal aneurysms. Virgil Scott. Am. J. Syph., Gonor. & Ven. Dis., St. Louis, 28: 682–710, Nov. 1944.

Aneurysm of the abdominal aorta and its branches has been much less completely studied than aneurysm of the thoracic aorta. The author reviews the literature and analyzes case histories and autopsy findings of 96 patients observed at Johns Hopkins Hospital. Diagnoses in all cases were proved by autopsy, by exploratory laparotomy, or by clinical and roentgenologic findings.

Among the entire 96 patients the etiology of the disease was syphilis in 58.3 percent, arteriosclerosis in 20.0 percent, bacterial agents (mycotic) in 18.8 percent. Periarteritis nodosa and tuberculosis caused aneurysm in 1 patient each.

A distinct relation was found between the site of the aneurysm and the causative agent. Thus, syphilis was the major cause of aneurysms of the upper abdominal aorta and of aneurysms arising at the origin of

he major upper branches (celiac axis and superior mesenteric artery). Aneurysms of the lower aorta and of other branches were rarely syphilitic; instead, they were arteriosclerotic (aorta), or mycotic (smaller branches).

Syphilitic aneurysms occurred most frequently in patients under 50 years of age, very rarely in those over 60, whereas all the arteriosclerotic aneurysms occurred in patients over 50, and the majority were in the age group over 60. The highest incidence of mycotic aneurysms was in the younger age groups.

The incidence of syphilitic aneurysms was highest in the Negro and in the male. Arteriosclerotic aneurysms in this series occurred only among patients of the white race and for the most part among males.

The symptomatology of abdominal aneurysm varies with differences in location and size. In the syphilitic group the most significant symptom was abdominal or back pain. This was characteristically most severe at night and relieved by change of position. The majority of arteriosclerotic aneurysms were asymptomatic. Clinical detection of the characteristic physical manifestations of abdominal aneurysm—a mass exhibiting an expansile pulsation, a palpable thrill, and an audible bruit—is also related to site and size. Of these signs the first was found most constantly in the syphilitic group.

The patients in this series with syphilitic abdominal aneurysms showed a high incidence of syphilitic involvement of the thoracic aorta and of the aortic leaflets—34 percent had saccular thoracic aneurysms and an additional 18 percent syphilitic aortic regurgitation.

The important roentgenologic findings were: (1) Erosion of the vertebral column resulting from pressure of the aneurysm, the vertebrae commonly involved being the eleventh dorsal through the second lumbar, and (2) the presence of calcium deposits in the wall of the aneurysmal mass.

The survival of patients with syphilitic abdominal aneurysm may be quite variable. Although 70 percent succumbed within 36 months after onset of symptoms, 17 percent survived more than 5 years. The case history of 1 patient who has survived for 28 years is reported.

Aneurysm of the abdominal aorta with rupture into duodenum. H. R. Pratt-Thomas. Am. J. Clin. Path., Baltimore, **14**: 405–412, July 1944.

The author presents 3 cases of aneurysm of the abdominal aorta, 2 of which were due to syphilis. The first case was that of a 31-year-old Negro waiter who was admitted to the hospital after fainting and falling to the sidewalk. He was incontinent of urine and feces and vomited about a quart of dark gelatinous material, presumably blood. He complained of slight epigastric pain which was partially relieved by lying on the left side. The lungs were clear, and the heart was normal. Just above and to the right of the umbilicus, was a clearly visible, pulsating mass 6 cm. in diameter, round, freely movable, smooth and firm. No bruit was heard over the mass. For 3 months, the patient had had occasional dull, aching epigastric pain which was aggravated by overeating and which radiated to the right flank and right lower chest. He had noticed the throbbing mass above the umbilicus. He had occasional nausea but no vomiting. His history showed a positive blood Wassermann reaction but no antisyphilitic therapy. He was treated for shock, but died 2 hours after admission, following a profuse rectal hemorrhage and circulatory collapse. Autopsy revealed a saccular aneurysm of the aorta at the level of the celiac and superior mesenteric arteries. The deep portion of the cavity communicated with the lumen of the duodenum through an eroded hemorraghic focus in the duodenal wall. Histologic examination showed the aneurysm wall to be made up of scarred aortic tissue with fibrous elements predominating. There were vascularization and perivascular cuffing of lymphocytes and plasma cells.

The second case was that of a 48-year-old Negro farmhand whose chief complaint was pain in the stomach. Four months before being admitted to the hospital, he had noticed a burning in the epigastrium which had progressed to pain and a month later

had become constant and radiated from the lumbar spine to his hips. Three weeks before admission to the hospital, he vomited all foods taken. He was severely constipated and occasionally passed blood in his stools. Four days before admission, the pain shifted from the back to the umbilical region, and there appeared a small, pulsating mass which grew steadily. He had lost 75 pounds in weight in 7 months. He gave a history of syphilis 10 years ago. Death occurred suddenly. Autopsy showed on the posterior wall of the third portion of the duodenum an ulcerated area 2 cm. in diameter in the center of a rounded mass which was compressing the duodenum and partially obstructing it. The base of the ulcer consisted of old and fresh blood clot, and a probe could be passed through the clot into an aneurysmal dilatation of the abdominal aorta. The aneurysm of the aorta, which was 5.5 cm. in diameter, was situated immediately below the mouths of the renal arteries. It was partially filled with layers of friable thrombus. The lining of the aorta about the margins of the aneurysmal opening showed longitudinal streaking and pearly thickening of the intima, as did the aortic lining about the mouth of the superior mesenteric artery. Histologic examination showed acute necrosis and polymorphonuclear infiltration in the aortic wall at the point of erosion into the duodenum.

Venereal diseases in India. J. Indian M. A., Calcutta, **8:** 269, June 1944.

It is difficult to assess the incidence of venereal disease in India. General public health measures and hospital facilities reach only a fraction of the population.

In 1919 when Iyenger performed Wassermann tests on 400 unselected apparently healthy Indian males, who were attending the Pasteur Institute of India, 22 percent were positive. In a series of 4,335 autopsies performed in the Department of Pathology and Bacteriology of the K. E. M. Hospital in Bombay there were 170 (3.9 percent) cases of cardiovascular syphilis, which represented 29.3 percent of the total of 578 cases of heart disease.

Next to smallpox, ophthalmia neonatorum takes second place as the major cause of blindness in India.

The venereal disease rate per 1,000 Indian troops increased from 18.9 in 1940 to 27.9 in 1941. The increase in 1940 more than doubled the 1939 rate, and that of 1941 was more than 3 times the highest rate recorded between 1929 and 1939.

TREATMENT

Modified intensive method for treatment of primary and secondary syphilis. Herman S. Zeve. U. S. Nav. M. Bull., Washington, **43:** 429–432, Sept. 1944.

A total of 142 patients with untreated primary or secondary syphilis received a modified intensive initial course of mapharsen therapy, consisting of an average of 10.5 treatments in 22.5 days (per man), without any evidence of increased risk above that encountered in less intensive methods. In addition, 0.13 gm. bismuth subsalicylate was given once a week. The majority of the infections were acquired in South American and Caribbean ports.

The average total dose of mapharsen each patient received was approximately 0.6 gm. The total number of treatments given was 1,494; the total number of treatment days required was 3,224. The number of days saved in relation to the single weekly method of treatment was 7,234, or 19.8 years; as compared with the biweekly method, 2,005, or 5.5 years.

It is the author's opinion that this method is more practical for military dispensaries and hospitals than the other more intensive methods now in use.

Combined fever and arsenotherapy in the intensive treatment of early syphilis. Evan W. Thomas and Gertrude Wexler. J.A.M.A., Chicago, **126:** 550–554, Oct. 28, 1944.

This paper reports the authors' experience in the intensive treatment of patients with early syphilis. Several large series of patients have been treated. In an early

series of 321 patients treated with mapharsen by multiple syringe injection, the incidence of encephalopathy was 1.6 percent and the fatality rate 0.3 percent. The addition of fever induced by typhoid vaccine with some reduction in the total amount of mapharsen was tried in 588 cases with no reduction in encephalopathy or fatality. In order further to reduce the total dose of mapharsen and the maximum single daily dose, a 10-day schedule was adopted which included 4 fevers and 4 injections of bismuth in addition to 10 injections of mapharsen, each approximately 1 mg. per kilogram of body weight. In a series of 1,181 patients treated on this schedule, 4 (0.34 percent) patients developed an encephalopathy and 1 (0.08 percent) died.

In evaluating the therapeutic results with the 10-day schedule, only patients followed for 6 months or more were considered. Among these, 80.7 percent had a favorable result, and 19.3 percent unfavorable. Included in the latter group were patients having a relapse or reinfection, or a Wassermann titer greater than 8 at last observation.

Treatment of early syphilis in 30 days. (Traitement de la syphilis recente en 30 jours.) A. Marin and A. Lambert. Union méd. du Canada, Montreal, **73:** 1031, 1944.

In the period from Jan. 1, 1942 to the end of September the authors have treated a total of 62 cases of early syphilis by means of daily injections of mapharsen given for a period of 30 days. In some cases the injections could not be given regularly because of certain reactions. The dosage used was 0.06 gm. mapharsen, regardless of sex and weight, making a total dose of 1,800 mg. for the 30-day period. Blood serologic tests were made before, during, and at the end of treatment. Spinal fluid examination was made whenever possible. The 62 cases consisted of 6 patients with seronegative primary, 22 with seropositive primary, 32 with early secondary, and 2 with late secondary syphilis. All of the patients were white; 29 were women and 33 were men; their ages varied between 7 and 56 years, the average age being 30 years. The 7-year-old child who was treated received two-thirds of the adult dose, a total of 1,200 mg.

Blood serologic reactions during the third month after treatment had been given showed the following results: 31 cases with originally positive serologic reactions had become seronegative; 5 cases of seronegative primary syphilis were still seronegative (the other patient with seronegative primary syphilis did not return for the test). In other words, 36 cases (51 percent) were negative at the end of treatment. However, 9 of these later showed positive blood serologic reactions.

Blood serologic reactions after an observation period of 24 to 32 months showed the following results: 27 cases (43 percent) remained seronegative; 17 patients on whom spinal fluid examinations were made showed negative results.

The reactions observed were erythema on the ninth day 4 cases (3 women, 1 man), icterus 1 case, granulocytopenia 13 cases; 12 of these were able to resume treatment after a week's rest and received a total of 1,800 mg. mapharsen.

Spinal cord level syndrome following intrathecal administration of magnesium sulfate for tabetic crisis. Samuel A. Guttman and Abner Wolf. Arch. Neurol. & Psychiat., Chicago, **52:** 135–139, Aug. 1944.

A metal worker, male, aged 53 years, received antisyphilitic therapy following a tabetic crisis in 1939. During another crisis in September 1942, a lumbar puncture was performed, magnesium sulfate was administered, and the crisis subsided. This was repeated on Feb. 10, 1943, following a third crisis, and a few hours later the patient experienced a peripheral vascular collapse, became irrational and had a temperature ranging from 104° to 107°F. for about a day. Several hours after the magnesium sulfate therapy, the patient had extremely severe shooting pains in his legs and feet and could not move them, nor could he void. Admitted to the Neurological Institute of New York on February 25, he appeared chronically ill, confused and disoriented. Neurologic examination showed

gross tremor of hands, paresis and areflexia of the lower extremities. There were hypesthesia, hypalgesia and hypothermesthesia in and below the first lumbar dermatome, and this involved the saddle region. The Wassermann reaction of the spinal fluid was positive in practically all dilutions, while the colloidal gold curve was 2211100000. The patient received a course of malarial therapy after which the flaccid paralysis of the lower extremities persisted, as did the level of sensory loss. The patient died about three months after the second intrathecal injection of magnesium sulfate.

Autopsy revealed no evidence of mechanical injury to the spinal cord or the cauda equina. There was marginal degeneration of the white matter with gliosis and foci of necrosis in the tips of the gray horns in the lower thoracic, lumbar, and sacral segments of the spinal cord. The nerve roots at these levels showed scattered focal areas of degeneration. The authors conclude that this method of therapy has certain dangers and is sufficiently hazardous to warrant caution in clinical application.

The acute toxicity of commercial penicillin. Henry Welch, Clifford W. Price, Jean K. Nielsen and Albert G. Hunter. J. Lab. & Clin. Med., St. Louis, **29**: 809–814, Aug. 1944.

A study of over 300 lots of penicillin sodium produced by 14 manufacturers showed that all passed the mouse safety-test. There is a wide variation in the acute toxicity of different manufacturers' products. Some products are lethal for mice in doses of 3,500 to 5,000 units, while one manufacturer is producing penicillin sodium lethal only at doses of 25,000 to 32,000 units.

A comparison of commercial samples of of penicillin calcium and penicillin sodium made from a single master lot showed the calcium salt to be by far the more toxic preparation. The greater toxicity of the calcium over the sodium salt of penicillin should not discourage its clinical use in man. The toxicity of the penicillin calcium is primarily due to the cation.

The toxicity of high potency samples of penicillin sodium and high or low potency samples of penicillin magnesium is due primarily to the cation used in producing these preparations. Similarly, the cation contributes substantially to the toxicity of penicillin ammonium.

The treatment of neurosyphilis. Harry C. Solomon, Joseph Earle Moore, Paul A. O'Leary, John H. Stokes and Evan W. Thomas. Bull. U. S. Army M. Dept., Carlisle Barracks, No. **82**: 66–76, Nov. 1944.

This article is intended to serve as a guide to the treatment of neurosyphilis by Army medical officers. The types of neurosyphilis met with in military practice are described and the various methods of treatment are discussed. The treatment of special forms of neurosyphilis is outlined in accordance with the recommendations of War Department Technical Bulletin TB MED 48, May 31, 1944, "Management of Neurosyphilis." This treatment is intended to provide for reasonable standardization under military conditions and for the maximum benefit of treatment which can be secured by hospitalization in a general hospital not to exceed 3 months. The results to be expected from the foregoing methods of treatment are discussed.

Systemic manifestations of bismuth toxicity. Albert Heyman. Am. J. Syph., Gonor. & Ven. Dis., St. Louis, **28**: 721–731, Nov. 1944.

This paper presents a review of the literature on bismuth poisoning and reports observations on 4 patients with severe systemic manifestations and renal insufficiency following bismuth therapy.

Bismuth melanosis of the large intestine and bismuth cervicovaginitis occurred in 2 of the cases, and the author states that the small number of such conditions reported may be due to the neglect of visual examination of the rectal and vaginal mucosa rather than to their rare occurrence. Careful search for this condition is indicated in all patients with bismuth intoxication.

Renal insufficiency following bismuth was a constant feature of these cases and also of many of those reported in the literature. This was manifested by anuria,

zotemia, albuminuria, and decreased henolsulfonphthalein excretion. The renal sions in these patients were very similar o those produced in animals by experimentation.

That preexistent renal damage may be a redisposing factor in bismuth poisoning as been discussed in the literature. In all of the patients described in this paper, the ephrotoxic action of the drug produced n intensification of a previous renal insufficiency. In 2 of them, the effect was emporary, and a fair degree of renal function returned after several months. In the other 2, death resulted from the combination of bismuth intoxication and previously existing vascular damage. Considerable caution in the use of bismuth in patients with previous vascular disease is necessary.

Severe toxicity and death caused by sulfathiazole: a case report and necropsy findings. C. F. Vilter and I. M. Scheinker. Ohio State M. J., Columbus, **40**: 1057-1060, Nov. 1944.

This paper presents the history and autopsy findings of a case in which the patient, a 33-year-old white man, died following sulfathiazole treatment for gonorrhea. Microscopic examination of tissues showed that the most uniform pathologic process consisted of small areas of focal necrosis, associated with proliferative changes of the interstitial tissue widely disseminated throughout the liver, kidney, lung, and adrenals. The histopathologic lesions encountered in the central nervous system consisted of vasoparalysis, petechial hemorrhages, and secondary parenchymal changes in the form of moderate degree of edema and glial cell proliferation. A diagnosis of sulfathiazole toxicosis was made.

The authors comment that an undue reaction to sulfonamide which causes death, though less common than mechanical interference with the kidneys, is apparently increasing in frequency. In this case the patient expired 48 hours after the appearance of the symptoms of sulfonamide intoxication despite the discontinuance of the drug at the first significant sign. The type of reaction elicited would not indicate that the blood level of sulfathiazole was too high, but rather that some drug was retained even in the absence of oliguria. In addition to the early miliary focal areas of necrosis scattered throughout the organs, there was also substantial evidence of severe encephalopathy and subarachnoid hemorrhage. Although all of the organs were not available for microscopic study, the nature and distribution of the lesions would indicate a generalized toxic reaction.

Clinicopathologic studies of renal damage due to sulfonamide compounds. Francis D. Murphy, Joseph F. Kuzma, Theodore F. Polley and John Grill. Arch. Int. Med., Chicago, **73**: 433–434, June 1944.

This article presents a study of clinical and pathologic data in 14 cases of renal insufficiency due to intoxication with sulfonamide compounds. Thirteen of the 14 patients died and were studied post mortem. Decapsulation of the kidney was done and a biopsy specimen taken in the case of 1 patient who recovered.

Most of the commonly prescribed sulfonamide compounds were employed, but sulfathiazole was used most frequently.

In a few of the cases deposits of crystals of the drugs in the urinary tract causing some degree of mechanical obstruction were found associated with the nephrotoxic lesion; but this was not the rule, as in most of the cases reported the nephrotoxic lesion was independent of mechanical blocking.

Histologically there was simple tubular degeneration present in all the kidneys regardless of what other changes were present. Advanced tubular degeneration, necrosis of the tubular cells and intense inflammatory reaction outside the nephron in the surrounding tissues occurred in some cases. These various tubular lesions undoubtedly represent degrees in the severity of one process rather than different kinds of response. In 1 case advanced changes in the glomeruli are reported.

No correlation between the clinical features and the specific site for the renal tubular damage was determined in this study.

The toxic reactions of the newer sulfonamides. Carl F. Vilter and M. A. Blankenhorn. J. A. M. A., Chicago, 126: 691-694, Nov. 11, 1944.

The toxic reactions observed among 1,936 patients treated in the Cincinnati General Hospital with sulfathiazole, sulfadiazine, sulfapyrazine, sulfaguanidine and succinylsulfathiazole are analyzed. Sulfapyridine is considered obsolete and is no longer used in this service; sulfanilamide is rarely employed, and only a preliminary report could be given on sulfamerazine.

It was found that untoward reactions caused by sulfadiazine were significantly less frequent than those due to sulfathiazole or sulfapyrazine. The symptomatology observed is described in detail. The disorders included fever, skin lesions, conjunctivitis, nausea and vomiting, polyneuritis, delirium, polyarthritis and arthralgia, alterations of the blood and bone marrow. Most of these were not very troublesome and, with the exception of neuritis, disappeared within 2 or 3 days of discontinuance of the drug. The most troublesome complications centered about the kidney and urinary tract, all of the 11 deaths observed being mainly due to nephrosis. The findings in and treatment of this condition are discussed in detail. It was concluded that with advanced age and renal disease, sulfonamides should be prescribed cautiously and treatment followed carefully, and that the early signs of severe reactions are so occult as to be revealed usually only by laboratory studies.

Lumbar puncture headaches. Myron J. Levin. Bull. U. S. Army M. Dept., Carlisle Barracks. No. 82: 107–110, Nov. 1944.

During a 5½-month period, lumbar spinal punctures were performed on 2,217 syphilitic candidates for induction into the Armed Forces. The fluids were collected rapidly; the patients got on their feet immediately, and were instructed to keep active and not to lie down. Only 15 cases (less than 1 percent) of postpuncture headache severe enough to require bed rest were reported; these patients responded to from 1 to 3 days of bed rest and liquid diet.

Rapid collection of spinal fluid and maintenance of the erect position after spinal puncture apparently decreased the number of headaches in this series. This is believed to be due to the more nearly normal intracranial pressure maintained by the erect position, thus preventing oversecretion and compensatory hypertension with resultant headache.

Penicillin in sulfonamide-resistant gonorrhea. Preliminary report of 124 cases. John G. Menville and Clarence W. Ross. U. S. Nav. M. Bull. Washington, 43: 423–428, Sept. 1944.

One hundred and twenty-four patients with sulfonamide resistant gonorrhea were apparently cured by penicillin, although the response to the drug was not uniform, and the treatment had to be individualized by trial and error methods in estimating dosages.

Of the 124 patients, 118 were white and 6 Negroes; the average age was 21.7 years. Eighty-three patients responded to single courses of the drug, and 41 to multiple courses. There were complications in 31 cases; epididymitis developed in 2 patients after 2 or more courses of penicillin.

In the noncomplicated cases, 100,000 units of penicillin were administered intramuscularly in 15,000-unit doses every 3 hours. In all complicated cases where early failures occurred, intravenous and intramuscular routes were adopted. The routine daily dosage was 100,000 units given intravenously in 2,000 or 3,000 cc. isotonic saline as a continuous drip for 24 hours. During this interval, 200,000 units were given intramuscularly in 20,000-unit doses every 3 hours and the 2 doses which remained were administered the following day. Using this schedule as a criterion for a day's treatment, the following scale is used: Prostatitis, 1 day; epididymitis, 2 days; periurethral abscess, 2 to 3 days, and arthritis, 3 to 5 days (in addition, in arthritis, local instillation into the joint is used daily).

The criteria of cure are 7 consecutive

ily negative urethral spreads and 3 consecutive negative prostatic cultures. Some of the apparently cured patients were not released from the hospital immediately, and 9 patients of this apparently cured group presented delayed positive spreads for gonorrhea; in 1 of these patients, 6 consecutive negative spreads were observed before a delayed positive spread occurred. In 9 of these cases, the original dose of penicillin was 50,000 units or less, and in 1, a delayed positive spread occurred after an initial dose of 160,000 units of penicillin.

The authors feel that while a connection exists between a delayed positive spread and a small initial dose of penicillin, there is, in certain cases, a partial immunity to penicillin, either in the host or in the strain of gonococcus.

Use of penicillin for gonorrhea resistant to sulfonamide compounds. Leander W. Riba, Carl J. Schmidlapp and Nathaniel L. Bosworth. War Med., Chicago, 6: 72–79, Aug. 1944.

The authors studied the results in the treatment with penicillin of 450 patients with sulfonamide resistant gonorrhea. Group 1 of 105 patients treated with 160,000 units had 2 (2 percent) failures; group 2 of 112 patients treated with 100,000 units had 11 (9.8 percent) failures, and group 3, of 233 patients treated with 50,000 units had 55 (23.6 percent) failures. All patients had previously received sulfonamide compounds, chiefly sulfathiazole and sulfadiazine, by mouth, in an average of 85 gm. each, without clinical cure. A detailed statement of the pretreatment examination of urine, urethral discharge, and gram-stained spreads and cultures is given. Not all colonies of gonococci which elicited positive oxidase reactions were checked with sugar fermentation tests. Resultant complications are listed and treatment commented upon. Loss of manpower days due to the infection is tabulated; results of posttreatment laboratory examinations are discussed and charted; detailed case reports are given in each of the 14 failures.

The authors conclude that the action of penicillin is bacteriostatic rather than bacteriocidal and that the resultant attenuation of gonococci may cause failures to be dismissed as cures to become gonococcus carriers. Treatment with insufficient doses of the drug contributes to this effect. The use of penicillin in the treatment of gonorrhea frequently masks the presence of primary syphilis. A total of 160,000 units of penicillin approaches the optimum maximum dose necessary to clear the highest percentage (98 percent) of resistant gonorrheal infections in male patients. The amount of each dose and the interval of injection merit further investigation.

Sulfonamide therapy of gonorrhea. Ruth Boring Thomas, William E. Graham and George R. Cannefax. J. A. M. A., Chicago, 126: 623–625, Nov. 4, 1944.

The results of sulfonamide therapy of gonorrhea among 555 women patients, all of whom were institutionalized until considered cured, are reported.

The patients, 200 of whom were Negro and 355 white, were treated for culture positive gonorrhea at the U. S. Public Health Service Medical Center, Hot Springs, Ark. The mean age of the group was 20 years. Because of the presence of local inflammations and of the vague histories obtainable, it was generally impossible to date the onset of the gonococcic infection or to determine its stage. However, few cases were considered acute. Bacteriologic tests for gonococci were performed on admission and thereafter every other day, if negative, until a total of 6 had been taken. Cultures were routinely performed but positive findings were confirmed by sugar fermentations only in exceptional cases. Treatment was instituted only after at least one demonstration of gonococci by culture.

Most patients received sulfathiazole in either of 2 systems: 1 gm. 4 times daily for 5 days, or 2 gm. 4 times daily for 2 days and then 4 gm. daily for 3 days. Five days following the completion of a drug course, the first test of cure was made. If the culture was still positive and the white blood cell count not unduly depressed, a second course was given. Failures following the second course were considered sulfonamide resistant. In a few instances,

a third course was given alone, but usually other measures were tried, such as a sulfonamide combined with nonspecific protein therapy. Artificial fever was used for 25 patients. After penicillin became available, it was used in injections of 10,000 units every 3 hours for a total of 60,000 units, and failures received 20,000 units every 3 hours for a total of 120,000.

Negro patients responded to treatment more readily than did white ones. All the patients receiving artificial fever were white, as were all but one of those for whom penicillin was used.

The results correspond closely to those recently reported with both Negro and white men in the Army. Explanation of the difference in response between Negro and white patients awaits further study.

There was no significant difference between the final results produced by the 2 methods of administering sulfonamides, though the large dosage showed the higher incidence of reactions. Reactions were few and usually mild. Four instances of conjunctivitis occurred. The only serious reactions were 3 instances of ureteral blocking, all of which occurred in patients on the intensive dosage, and relatively early in the course.

Sulfonamide resistant gonorrhea. (Die sulfonamidresistente Gonorrhoe.) J. Wiederkehr. Praxis, Bern, 33: 247–251, 1944.

The situation in regard to the treatment of gonorrhea has changed greatly in the past 2 years. In the period 1940 to 1941 the percentage of cures reported was nearly 100 percent and hope was expressed that gonorrhea could be completely eradicated by means of sulfonamide drugs. Gradually, however, it was noted that the number of cases which did not respond to sulfonamide therapy was progressively increasing. Of a total of 542 cases of gonorrhea treated during the period 1942 to 1943 at the city polyclinic in Zurich only 36.4 percent of those treated during the last 3 months of this period were cured with one course of sulfathiazole (cibazol) ; 38.6 percent of the cases failed to respond to several courses of sulfathiazole combined in some cases with fever therapy; in these cases local therapy had to be used. Similar observations of sulfonamide failure have been made by Olin (Finland), Krantz and others (Germany) and Juon, Storck and Dracl (Switzerland). Bacteriologic studies have shown that this lack of response to therapy is due chiefly to increased resistance of the gonococci to sulfonamides. It was found that sexual partners who were infected with the same strain of gonococcus usually reacted in a similar manner to sulfonamide therapy. Of 71 patients treated whose sexual partners were treated simultaneously the infection in 60 partners responded in a manner similar to that of the patient whereas in 11 the response was different. Because of these observations, careful follow-up with provocative tests is of great importance.

Toxic hepatitis in fever therapy. Robert M. MacDonald. Canad. M. A. J. Montreal, 51: 445–449, Nov. 1944.

The author reports the occurrence of 48 cases of toxic hepatitis in 250 healthy young male patients treated with fever chemotherapy for sulfonamide resistant gonorrhea. Five cases were considered marked jaundice, 6 were moderate, and the remaining 37 were mild or doubtful.

Anoxia may have played some part in the etiology but the chief factor in the production of jaundice in the present series appears to have been the effect of high body temperature on the liver in patients who had a relatively high blood sulfonamide level. The author has not observed this complication in the treatment at about 105° F. of patients with neurosyphilis, nor in the 21 cases in the present series whose treatment was terminated before 7 hours was completed. Of the 16 patients with previous toxic reactions to sulfonamides who received fever therapy without chemotherapy, none developed jaundice, though one had an icteric index of 20 on the first day after fever.

The author recommends the giving of large amounts of protein for 2 days before treatment, keeping the temperature at 106° F. and the liberal use of oxygen, as protective measures.

LABORATORY RESEARCH

urther observations on the relation of the eye to immunity in experimental syphilis. II. The development of immunity after primary intracorneal inoculation. Alan M. Chesney and Alan C. Woods. J. Exper. Med., Baltimore, **80**: 357–367, Nov. 1944.

The authors report two experiments de-gned to determine whether a primary oculation of syphilitic virus into the rneas of normal rabbits is followed by .) the development of a general immunity ward the infection as manifested by a gative response to a subsequent inocula-on of homologous syphilitic virus made to the skin, and (2) by the development local immunity in the cornea itself.

Female rabbits were inoculated intra-rneally with a virulent strain of Trepo-:ma pallidum and the disease was allowed run its course until the lesions which ad developed at the site of the inoculation ad healed spontaneously. Popliteal lymph odes were transferred from about one-alf of these animals (in the second experi-ent only) to normal male rabbits and by is method the nodes were proved in most nstances to contain virulent treponemes, nowing that generalization of the syphilitic fection is the rule after intracorneal noculation. All animals were treated with rsphenamine after the local lesion had ubsided (160 to 275 days after the original noculation). The rabbits were then re-noculated with the homologous strain of reponemes, injections being made into the ornea originally inoculated and into the kin of the back.

In one-half of all the test animals both ornea and skin were immune to a second noculation of homologous syphilitic virus. n addition to these there were 5 animals n which the cornea was immune and the kin nearly so. Thus, in two-thirds of the nimals there developed in both skin and the cornea, after primary intracorneal inoculation, a high degree of resistance toward a second inoculation with homologous syphilitic virus, but syphilitic disease of the cornea does not always impart to the cornea itself an absolute immunity to reinoculated homologous virus.

Further observations on the relation of the eye to immunity in experimental syphilis. III. The influence of a nonspecific in inflammatory reaction in the cornea on the development of immunity in that tissue after intratesticular inoculation. Alan M. Chesney and Alan C. Woods. J. Exper. Med., Baltimore, **80**: 369–375, Nov. 1944.

This paper reports two experiments designed to test the hypothesis that local avascularity of the cornea may be responsible for the failure of that structure to become immune during the course of syphilitic infection. To this end the corneas of treated syphilitic rabbits were rendered vascular through the establishment of a nonspecific inflammatory reaction. After the acute manifestations of inflammation had subsided, both corneas were tested for immunity to homologous syphilitic virus.

The results of the two experiments were similar and while they were not conclusive, they indicated that there was a tendency for corneas which had been injected with dead tubercle bacilli to be more refractory to a subsequent inoculation with homologous syphilitic virus than the corneas of the same animals that had not been so injected. This tendency may be interpreted as suggestive evidence for the view that in the syphilitic rabbit there develops circulating antibodies toward the homologous strain of Treponema pallidum.

The local chemical prophylaxis of experimental syphilis with phenyl arsenoxides. Harry Eagle, Ralph B. Hogan and Ralph Fleischman. Am. J. Syph., Gonor. & Ven. Dis., St. Louis, **28**: 661–681, Nov. 1944.

Nine trivalent arsenicals were studied with respect to their local chemical prophylactic activity in rabbit syphilis. All

were shown to be of value but the efficacy of individual compounds was in proportion to their direct treponemicidal action in vitro. The effective concentration varied with the time interval between inoculation and application.

Methods and materials employed were discussed in detail.

Local prophylaxis did not give rise to symptomless infections, and it was found that the failure of a lesion to develop at the site of inoculation could be taken as prima facie evidence of successful prophylaxis.

The arsenicals were shown to owe their prophylactic activity to a direct action on the spirochetes in the skin itself. The arsenicals did not penetrate to adjacent lymph nodes.

The stability of the selected compounds here discussed, the time interval over which they remain effective, the low concentrations necessary within reasonable time periods, and the absence of local irritative effects at those concentrations, all offer promise that some of these compounds may be of value in the prophylaxis of the human disease.

Studies on the incidence and nature of false positive serologic reactions for syphilis. Charles R. Rein and Elizabeth S. Elsberg. Am. J. Clin. Path., Baltimore, **14**: 461–469, Sept. 1944.

General considerations in the occurrence of false positive serologic reactions for syphilis are reviewed, and their increasing importance pointed out. False positive reactions are divided into 3 types: technical, syphiloid, and biologic; each of these is described and its causes discussed.

Most of the paper is concerned with the biologic false positives. Data collected by the authors are presented concerning their frequency among serums from patients with vaccinia, upper respiratory infections, leprosy, filariasis, Weil's disease, malaria, and typhus. The incidence of false positives in these diseases ranged from 11.3 percent in filariasis to 85 percent in leprosy.

The various verification procedures which have been developed are reviewed and a set of requirements which should be met by a satisfactory verification test is given. The authors conclude that no verification test in use at the present time is satisfactory. Various factors in the development of false positive tests are discussed, and procedures are suggested for establishing the true nature of repeated positive and doubtful reactions met with in individuals who present no confirmatory history or physical findings.

Biologic false positive serologic blood tests following stimulating dose of tetanus toxoid. Leonard L. Heimoff. Mil. Surgeon, Washington, **95**: 419–421, Nov. 1944.

Stimulating doses of tetanus toxoid are apparently capable of causing biologic false positive serologic reactions for syphilis. The author reports 8 cases of biologic false positive serologic reactions, all of them in soldiers, who applied for premarital blood tests shortly after having received stimulating doses of tetanus toxoid. All denied any history of penile lesions or recent febrile illnesses, and none presented any clinical evidence of syphilis. In 1 case there was a positive reaction to a Kahn test as early as 10 days after inoculation, and some remained positive as long as 10 weeks afterwards. All became negative without treatment within 12 weeks. Complement fixation tests remained negative or doubtful in all patients; spinal fluid tests were made in only 2 instances, and both of these were negative.

The effect of bile acids on the biliary excretion of neoarsphenamine and mapharsen. J. H. Annegers, F. E. Snapp, A. C. Ivy and A. J. Atkinson. J. Lab. & Clin. Med., St. Louis, **29**: 853–862, Aug. 1944.

This study carried out in dogs confirms by a more direct method the conclusion of other investigators that the liver is the predominant organ concerned with the excretion of arsensicals. Within 2 or 3 days after injection, from 30 to 60 percent of the arsenic administered as neoarsphenamine or mapharsen in well-tolerated doses is excreted in the bile. It appears that mapharsen arsenic is more rapidly excreted than

oarsphenamine arsenic. The simultane-
is intravenous administration of sodium
hydrocholate with neoarsphenamine de-
eases the rate of excretion of the arsenic
the bile, though a choleresis occurs. If
e administration of dehydrocholic acid
minishes the hepatotoxic action of neo-
sphenamine and mapharsen, it does not
so by increasing the excretion in the
le. The results of this investigation do
t provide a clear and substantial rationale
r the administration of bile salts with
senicals.

PUBLIC HEALTH ADMINISTRATION

Workmen's compensation acts: Gonorrheal infection in eyes weakened by industrial injury compensable. J. A. M. A., Chicago, **126**: 387, Oct. 7, 1944.

In the course of employment on Apr. 30, 942 some fluid used for a wood preservative splashed up into an employee's face nd eyes. He was treated immediately and gain the next day, being discharged on May 3 as able to work. Two days later he employee returned to the physician, and is right eye was found to be infected with 'gonorrheal germs." It is undisputed that he employee did not have any venereal disease and that the infection came from ome source other than the workman. The nfection spread to the left eye on May 8, nd as a result of the infection the employee ost the sight of his left eye. He instituted proceedings under the workmen's compensation act of Arkansas and was awarded compensation by the workmen's compensation commission.

The employer and his insurance carrier appealed to the circuit court, Phillips County, Ark., which affirmed the award of compensation. An appeal to the Supreme Court of Arkansas followed.

The court, believing that the commission was justified in finding that there was a causal connection between the original injury and the resulting blindness in the left eye and that compensation was properly awarded, accordingly affirmed the judgment in favor of the workman.

Social malaise and disorder. Views of the Medical Women's Federation. Brit. M. J., London, **No. 4373**: 571–572, Oct. 28, 1944.

This memorandum was approved by the Medical Women's Federation as expressing their views concerning the reported increase in venereal diseases in the British Isles. It states that the solution of the venereal disease control problem must depend in large measure upon a clear recognition of the relation of venereal disease to social and personal maladjustments. While the physician has an obligation to society for the treatment of a patient, he has also a duty to interest and educate public opinion in medicosocial questions so that these may be approached with understanding and sympathy.

In order to achieve stability of family life, education in its widest sense, training for suitable work, and encouragement in the right use of leisure, the Medical Women's Federation recommends: (1) Recognition of the vital importance of home and family life; (2) training from an early age in development of personal moral responsibility and social obligation, as well as religious training at home and at school; (3) extension of education into adult life, and (4) provision of suitable opportunities for social contacts and recreation.

New Cases of Syphilis and Gonorrhea in States, Territories and Possessions

Health officers' monthly statement: Reported for the first 4 months of fiscal years 1944-45 and 1943-44

Area	Cases of syphilis and gonorrhea reported for first 4 months of fiscal years below:											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44
Total United States†	[1]117,684	[1]162,835	[2]24,945	[2]26,595	[2]32,182	[2]43,869	[2]47,640	[2]69,783	[2]3,998	[2]4,746	[2]97,035	[1]106,250
Alabama	4,849	5,985	680	864	1,053	1,414	968	1,436	88	138	2,166	2,484
Arizona	(*)	1,044	(*)	238	(*)	274	(*)	404	(*)	45	(*)	603
Arkansas	2,966	2,946	617	406	942	1,025	1,107	1,069	85	73	1,927	1,551
California	9,574	10,789	1,742	1,728	2,156	2,556	5,216	5,937	301	330	11,427	10,572
Colorado	778	1,587	214	358	246	448	291	717	27	64	773	1,182
Connecticut	899	1,071	87	120	446	397	152	323	30	62	368	527
Delaware	245	321	51	34	74	71	99	44	9	5	87	64
Dist. Columbia	317	2,724	40	348	64	672	123	1,561	9	45	269	1,256
Florida	4,751	11,044	735	1,094	1,594	3,321	1,952	5,150	125	229	5,006	6,244
Georgia	3,792	6,220	1,052	1,136	1,504	2,575	1,102	2,315	134	192	2,654	4,086
Idaho	334	214	65	112	70	39	187	43	10	3	176	281
Illinois	7,458	9,454	1,245	1,167	1,737	2,299	4,250	5,782	226	206	7,221	8,537
Indiana	2,065	2,906	454	386	265	256	695	1,040	68	88	1,159	1,191
Iowa	516	855	115	177	127	222	226	361	29	65	858	654
Kansas	957	857	229	148	166	179	513	496	49	34	1,075	703
Kentucky	1,784	2,822	418	377	422	617	682	1,216	95	114	1,549	1,297
Louisiana	4,336	6,925	982	983	1,329	1,715	1,049	1,895	168	158	4,830	4,676
Maine	306	276	64	61	39	30	115	143	26	24	689	456
Maryland	2,900	5,755	631	545	712	570	715	897	63	48	1,640	3,147
Massachusetts	1,424	1,643	362	370	(§)	(§)	973	1,199	89	74	1,550	1,594
Michigan	6,029	6,303	1,009	851	1,679	1,584	2,187	2,659	159	166	4,225	3,875
Minnesota	720	881	115	85	66	93	491	631	27	49	878	693
Mississippi	7,318	9,161	2,490	3,187	2,051	2,549	2,339	3,032	438	393	10,956	10,285
Missouri	3,093	3,213	698	608	838	797	1,334	1,452	108	111	2,654	1,810
Montana	163	137	37	42	17	12	40	63	3	3	113	146
Nebraska	415	432	65	73	109	255	228	70	10	17	631	603
Nevada	148	305	42	8	1	49	60	222	6	10	221	140
New Hampshire	92	63	7	9	4	25	69	24	10	2	57	63
New Jersey	2,724	3,944	435	472	730	1,308	1,417	2,013	107	147	1,750	1,977
New Mexico	581	694	128	155	157	156	267	341	43	42	474	496
New York	9,854	13,116	1,984	1,896	1,980	2,249	5,532	8,469	257	365	4,798	6,715
North Carolina	3,039	4,088	1,135	1,065	1,158	1,607	684	1,331	62	85	3,491	3,293
North Dakota	79	95	16	29	9	18	33	32	4	4	130	105
Ohio	6,633	8,263	1,414	1,132	1,825	1,953	3,122	4,069	272	328	2,581	1,842
Oklahoma	2,178	2,831	374	363	565	829	742	1,033	75	116	2,517	1,713
Oregon	672	741	161	209	86	56	389	467	31	9	809	741
Pennsylvania	3,841	4,560	704	570	1,204	1,861	1,264	1,674	132	226	0	371
Rhode Island	303	365	82	23	26	36	141	273	13	7	661	274
South Carolina	3,025	5,900	790	1,190	1,003	2,534	995	1,912	110	149	2,436	2,298
South Dakota	(*)	168	(*)	32	(*)	27	(*)	74	(*)	14	(*)	149
Tennessee	5,049	6,496	780	927	1,948	2,667	2,009	2,681	143	144	4,121	5,750
Texas	5,404	8,042	1,090	1,075	1,875	2,319	1,951	3,001	208	216	3,339	3,885
Utah	201	325	63	79	13	44	122	195	3	7	212	220
Vermont	65	89	8	26	20	24	29	37	5	2	153	65
Virginia	3,205	4,970	969	1,563	1,303	1,822	834	1,378	74	102	1,817	4,458
Washington	1,354	1,506	297	273	313	386	541	601	28	50	1,715	2,954
West Virginia	679	1,434	192	225	89	178	124	271	15	32	813	897
Wisconsin	(*)	370	(*)	70	(*)	0	(*)	296	(*)	4	(*)	456
Wyoming	569	487	77	46	167	52	281	228	24	12	59	79
Territories, Possessions and Canal Zone												
Alaska	3	31	3	18	0	6	0	3	0	1	32	137
Canal Zone	38	(*)	3	(*)	8	(*)	24	(*)	1	(*)	38	(*)
Hawaii	275	289	92	59	34	34	131	178	12	17	608	524
Puerto Rico	627	6,836	110	637	207	1,389	156	2,174	136	828	329	1,345
Virgin Islands	11	78	2	18	8	44	1	12	0	4	6	126
Actual Total‡ U. S. and Possessions	118,638	171,651	25,155	27,667	32,439	45,643	47,952	72,924	4,147	5,659	98,048	109,590

* Data not available.
** Includes "not stated."
† Based on States reporting in both fiscal periods.
‡ Includes all reported cases.
§ Included in late latent.
[1] Based on 46 States.

New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over

Health officers' monthly statement: Reported for the first 4 months of fiscal years 1944-45 and 1943-44

City	Cases of syphilis and gonorrhea reported for first 4 months of fiscal years below:											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44
Total†	[1]34,450	[1]50,989	[2]7,219	[2]5,612	[2]7,745	[2]10,672	[2]14,965	[2]22,148	[2]833	[2]978	[3]22,761	[3]20,548
Akron	340	330	90	41	70	81	154	192	26	16	226	123
Atlanta	889	1,136	248	248	261	343	369	534	11	13	1,136	402
Baltimore	1,936	4,688	538	420	481	386	607	690	27	27	967	1,146
Birmingham	1,106	1,833	125	115	294	498	271	435	29	30	199	189
Boston	530	611	125	133	80	0	263	381	22	11	535	453
Buffalo	(*)	621	(*)	68	(*)	106	(*)	431	(*)	16	(*)	295
Chicago	(*)	4,720	(*)	743	(*)	1,196	(*)	2,667	(*)	114	(*)	4,562
Cincinnati	796	1,118	142	146	(§)	(§)	654	972	0	0	375	371
Cleveland	1,483	1,414	310	230	469	480	672	671	32	33	639	496
Columbus	483	526	142	91	114	109	212	291	15	15	177	117
Dallas	(*)	831	(*)	166	(*)	167	(*)	491	(*)	7	(*)	267
Dayton	367	664	46	62	126	190	182	386	13	26	199	215
Denver	345	736	95	137	117	190	113	281	7	19	302	634
Detroit	3,391	4,444	644	521	1,177	1,363	1,499	2,480	71	80	1,990	2,109
Honolulu	87	177	24	34	11	23	46	107	3	13	384	379
Houston	578	653	132	106	221	232	201	292	24	23	754	801
Indianapolis	626	737	138	255	80	5	153	152	7	8	193	40
Jersey City	127	205	15	19	37	44	67	138	8	14	28	17
Kansas City	479	629	97	105	109	98	237	396	23	28	347	331
Los Angeles	3,760	3,878	1,168	0	399	1,502	2,070	2,264	123	112	2,305	1,667
Louisville	414	881	122	116	82	158	177	361	17	7	440	316
Memphis	(*)	2,322	(*)	204	(*)	1,122	(*)	968	(*)	28	(*)	2,076
Milwaukee	172	166	29	19	0	0	139	133	5	1	151	81
Minneapolis	190	230	54	45	30	39	102	140	4	5	377	276
Newark	564	761	118	94	190	202	253	449	13	16	408	316
New Orleans	(*)	705	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	302
New York	6,888	9,057	1,610	1,507	1,690	2,020	3,350	5,221	167	225	4,798	4,703
Oakland	533	517	66	60	120	122	301	322	13	10	576	391
Oklahoma City	442	663	109	75	123	213	130	244	9	12	425	307
Omaha	165	203	27	16	30	140	103	33	5	14	153	191
Philadelphia	1,891	3,868	250	130	337	493	439	619	35	48	296	263
Pittsburgh	527	2,891	85	(*)	141	(*)	272	(*)	29	(*)	102	(*)
Portland	(*)	345	(*)	81	(*)	22	(*)	242	(*)	0	(*)	310
Providence	146	178	15	44	17	9	82	113	6	4	50	60
Rochester	97	81	24	14	6	7	66	57	1	3	151	98
St. Louis	1,962	1,805	413	270	611	625	880	846	58	54	1,397	528
St. Paul	72	110	15	14	14	22	34	64	2	3	98	117
San Antonio	438	393	38	43	85	102	209	230	12	16	313	439
San Diego	495	465	64	37	144	123	232	285	22	17	420	300
San Francisco	916	1,055	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	875	731
Seattle	485	443	110	50	119	90	244	269	5	8	599	533
Syracuse	225	364	17	9	12	16	194	327	2	12	159	106
Toledo	188	355	19	58	25	75	137	212	7	10	66	46
Washington, D. C.	317	2,724	40	348	64	672	123	1,561	9	45	253	1,256
Actual Total‡	34,450	60,533	7,304	6,874	7,886	13,285	15,237	26,947	862	1,143	22,863	28,360

* Data not available.
** Includes "not stated."
† Based on cities reporting in both fiscal periods.
‡ Includes all reported cases.
§ Included in late latent.

[1] Based on 38 cities.
[2] Based on 36 cities.
[3] Based on 37 cities.

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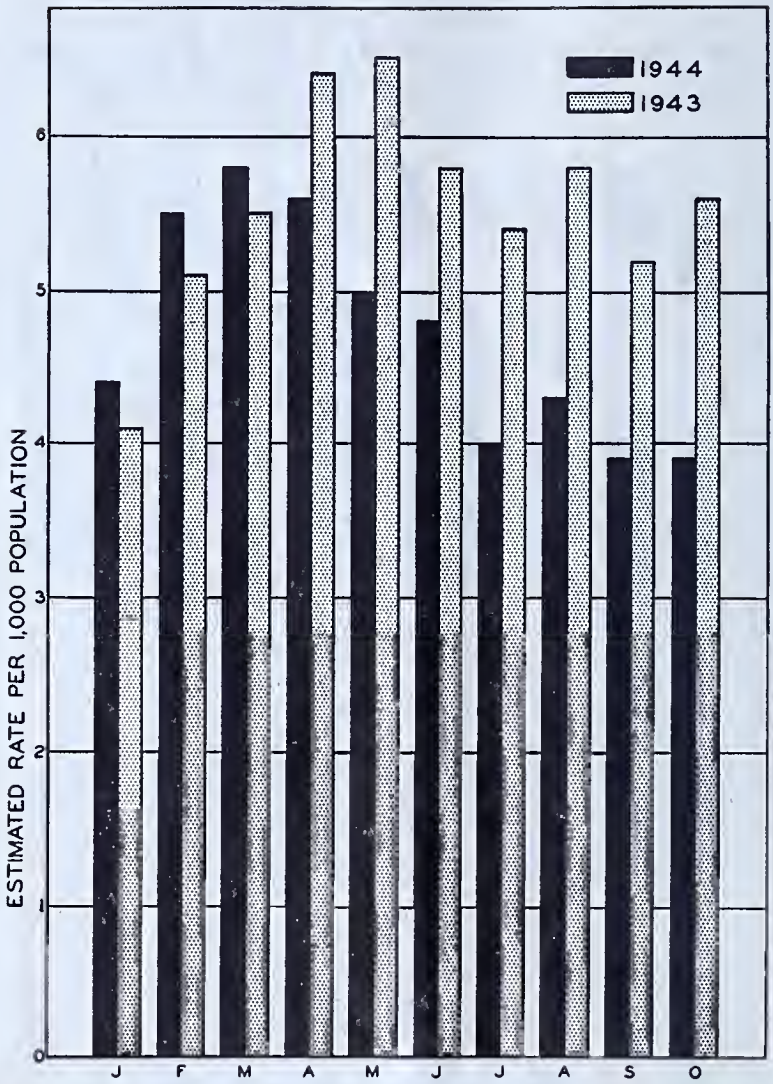

ANNUAL SYPHILIS CASE RATES IN CITIES OF 200,000 POPULATION AND OVER, BASED ON PROVISIONAL MONTHLY DATA 1944 AND 1943

Venereal Disease Information

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THOMAS PARRAN, *Surgeon General*

Editor: J. R. HELLER, Jr., *Medical Director*
Chief, Venereal Disease Division

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Penicillin Therapy of Sulfonamide Resistant Gonorrhea in Women

Everett T. Duncan, Passed Assistant Surgeon (R)[1], Robert L. Zobel, Passed Assistant Surgeon[2], United States Public Health Service, and Robert H. Hutcheson, M.D.[3]

Recent reports as to the efficacy of penicillin in the treatment of sulfonamide resistant gonococcic infections were received with much enthusiasm. These wholly gratifying results have not been experienced by us in the treatment of female patients. This report deals with the first 40 female patients we treated with penicillin for sulfonamide resistant gonorrhea.

Recent publications (*1, 2, 3, 4, 5, 6*) have reported remarkable success in the treatment of gonococcic infections in males. Cohn and coworkers (*7*) reported 44 cases of sulfonamide resistant gonococcic infections in females treated with penicillin. He had 43 successful cases and 1 failure, using a dosage of 50,000 to 100,000 Oxford units (O. u.). The one failure received 50,000 O. u. but responded to a second course of 100,000 O. u. Cook and his associates (*3*) reported successful treatment of 3 female patients.

CASES STUDIED

Forty female patients who were hospitalized at the Middle Tennessee Medical Center proved to have sulfonamide resistant gonococcic infections and were treated with penicillin. All of them had received at least one course of sulfathiazole, grams one, four times daily for 5 days, with rest in bed. Thirty-two of these cases responded to the first course of penicillin therapy, but spreads and cultures of the other 8 patients continued to reveal gram-negative diplococci. These 8 cases were retreated successfully as noted below. Of the 32 cases that responded satisfactorily to the initial treatment, 2 were pregnant, the pregnancy being of 3 and 5 months' duration, respectively, and 3 had symptoms of salpingitis at the time treatment was started. The sole complication among the 8 failures was a case of Gartner's duct cyst. Thirty-five of the patients were white and 5 were Negro.

DOSAGE

Sodium salt of penicillin was dissolved in sterile water so that each cubic centimeter contained 10,000 O. u. This solution was given intramuscularly every 3 hours in doses of 20,000 O. u. for 7 injections and 1 injection of 10,000 O. u., for a total of 150,000 O. u.

CRITERIA OF CURE

All the patients had at least three clinical and laboratory examinations at 48-hour intervals. In taking our bacteriologic specimens, the cervical area was not only cleaned with swabs, but also a faucet suction was employed to remove the cervical mucus; pressure was then exerted with a bivalve speculum to obtain the fresh cervical secretion. All of the cultures reported here were positive with the oxidase test. The organisms so reported were not isolated and put through the sugar fermentation tests. However, in the interest of public health it was felt advisable to consider these cases as treatment failures. By the same token, a positive spread was also considered a treatment failure. The laboratory work (spreads and cultures) was performed by the Tennessee Department of Public Health.

RESULTS

Eight cases out of the total of 40 treated with penicillin were found not to respond to the dosage of penicillin, as evidenced by positive bacteriologic findings. These positive findings were in evidence in one case as early as 3 days, but the rest were found

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4, 5, 6, 10 and 12 days after the termination of treatment.

In 2 of the failures, bacteriologic evidence was obtained from the urethra, in 5 from the cervix, and in 1 from both the cervix and urethra. Of these patients, 5 were white and 3 were Negro. The table shows the results of bacteriologic exam inations of the patients who failed respond to the first course of penicill therapy. Results from differential ca bohydrate fermentation tests are not avai able since organisms transplanted from th culture plates did not survive.

Summary of laboratory results on eight female sulfonamide resistant gonorrheal cas that failed to respond to 150,000 Oxford units of penicillin

Case No.	Race	Days after treatment first positive test was found	Laboratory reports			
			Cervix		Urethra	
			Culture	Spread	Culture	Spread
1	W	6	−	−	+	−
2	W	10	−	+	−	−
3	W	6	−	−	+	−
4	N	6	−	+	+	−
5	W	5	−	+	−	−
6	W	3	+	−	−	−
7	N	12	−	+	−	−
8	N	4	−	+	−	−

No great change in the cervical secretions was observed, but we attribute this to the frequency of Trichomonas infections. We encountered such infections in 58 percent of our cases. However, in some cases in which flakes of pus could initially be found in the cervical secretion, these flakes dramatically disappeared from the secretion after treatment.

Only 6 of our patients were observed after menstruation, and of these, 2 were failures.

SUBSEQUENT TREATMENT FAILURES

All of the patients who failed to respond to treatment with one course of 150,000 O. u. of penicillin were given subsequent treatment with penicillin, and all were rendered noninfectious as evidenced by bacteriologic studies. Seven of these failure cases responded to a second course of penicillin therapy of 200,000 O. u. The other treatment failure was the Negro girl with a Gartner's duct cyst. She was given a second course of 150,000 O. u. but this dosage also failed to produce cure. However, following the third course of 300,000 O. u. she responded favorably.

SUMMARY AND CONCLUSIONS

1. Forty sulfonamide resistant gono rheally infected female patients were treat with 150,000 Oxford units of penicillin.

2. Eight (20 percent) of these patien failed on the first course as evidenced b bacteriologic studies, but 7 responded favo ably to a second course – 200,000 unit The eighth patient was not cured by tv courses of 150,000 O. u. but did respor to a third course of 300,000 O. u.

3. Female patients should have caref follow-up examinations following penicill therapy.

4. From our experience, it appears th these female gonorrhea patients did n respond as favorably to penicillin thera as did the male patients reported by other

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Penicillin used was manufactured by Charles Pfizer and Co., Inc., New York, and John Wyeth and Brother, Inc., Reichel Division, Philadelphia, Pa.

The Treatment of Neurosyphilis by Continuous Infusion of Typhoid Vaccine

Albert Heyman, M.D.

hough hyperpyrexia has been pro- for many years by the injection of id vaccine, this form of fever therapy ot been the method of choice in the nent of neurosyphilis (*1*). The poor s that have been obtained in the treat- of neurosyphilis are not surprising the usual methods of vaccine admin- ion do not create temperatures of peutically effective height or duration. value of this form of fever therapy, ver, has been increased considerably cent years by the use of a continuous ion of typhoid organisms (*2, 3, 4*). this new technic prolonged periods gh fever similar to those produced by anical means can now be achieved. ring the past year and a half, we have ed 60 patients with neurosyphilis at rady Hospital by this infusion method satisfactory results. It is the pur- of this report to outline our technic accine administration, the problems ntered, and the results obtained from rpyrexia by this method.

comparison of the continuous drip the two-dose technic suggested by on (*5*) reveals several important dif- ices. The most striking advantage of nfusion method, as shown in figure 1, is the production of a prolonged febrile response at the same temperature level obtained by the older technic. There is, moreover, a less abrupt rise and fall in the temperature and the chill itself is less severe with the use of the clysis method. With experience one can obtain a fairly level temperature curve for as long as 10 hours or more with surprisingly few serious reactions.

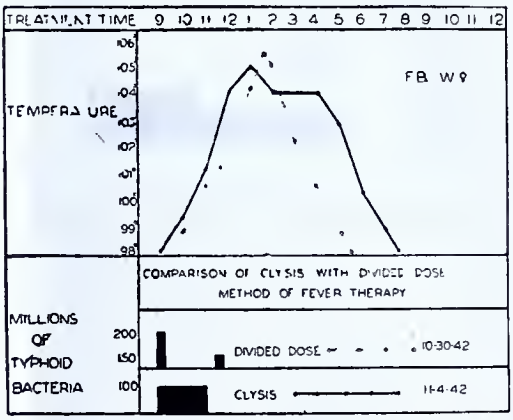


FIGURE 1.—Superimposed temperature charts comparing the responses of the double dose and clysis method of typhoid vaccine administration. The infusion contained one-half the number of organisms used in the single injections and was given to the same patient 4 days later.

We have chosen 50 hours of fever above 103° F. as a minimum course of fever therapy. To obtain this amount of hyperpyrexia, about 7 treatments are necessary, each consisting of approximately 7 hours above 103° F. Frequently, however, three-

m the Clinic for Genitoinfectious Diseases rady Hospital, the Department of Medicine mory University School of Medicine, and Georgia Department of Public Health, At- , Ga.

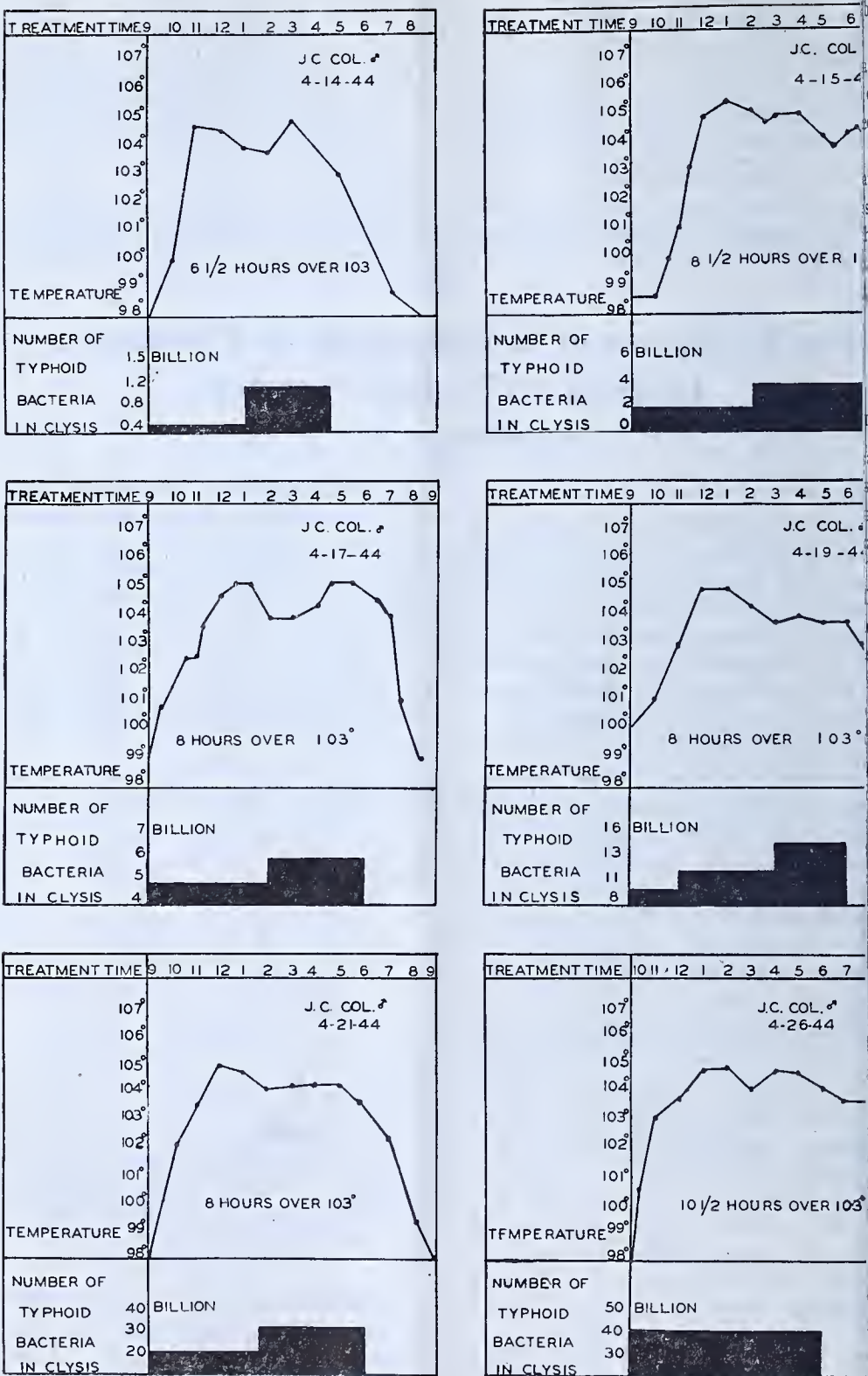


FIGURE 2.—Reproduction of the temperature charts showing a typical course of fever therapy ob by the clysis method of typhoid vaccine administration.

or more of the total number of
btained are above 104° F. Although
somewhat less than the optimum
dvised in artificial pyretotherapy
compares quite favorably with that
d by malaria (7); however, any
temperature level and duration may
ined by this method. Fever treat-
; given every other day and the
iospitalization period is less than
s. A week's rest at home is then
, after which the patient is permit-
return to work and is expected to
to the clinic for follow-up treat-

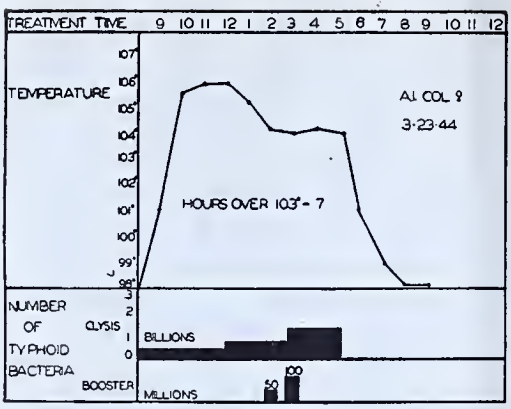
NIC OF VACCINE ADMINISTRATION

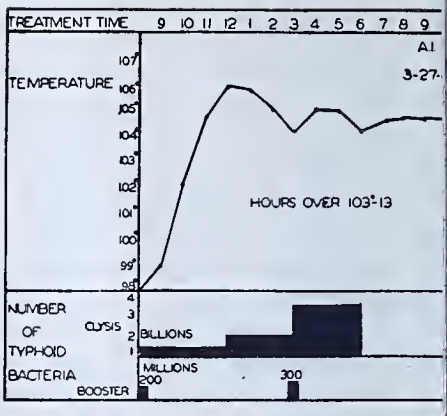
idmission to the hospital, each pa-
given a complete physical examina-
roentgen-ray examination of the
n electrocardiogram, and kidney and
inction studies. Urine examinations
ood counts are done on admission
re repeated frequently during the
of fever therapy.

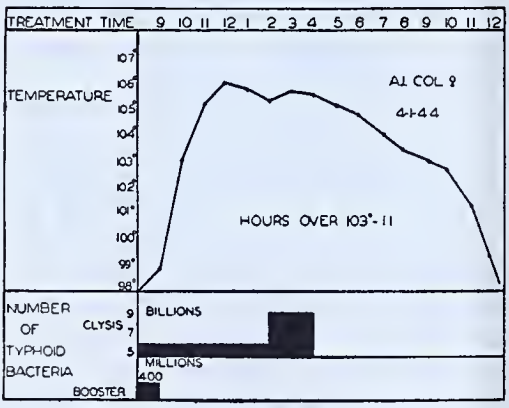
vaccine used is that distributed by
orgia Department of Public Health
munization purposes, and consists of
ension of approximately one billion
d organisms per cubic centimeter.
the active fever treatment is begun,
tient's sensitivity to the vaccine is
ined by the administration of 0.1
00 million organisms) of the vaccine
0 cc. of normal saline given over a
of several hours. Ordinarily this
amount of vaccine produces only a
febrile response, usually less than
., but an occasional patient will have
yed fever, sometimes as late as 24
after the clysis is completed. If no
sensitivity is exhibited, one-half to
illion organisms are added to a liter
rmal saline and given intravenously
e following day, at the rate of 50
per minute. Within 2 hours the pa-
has a chill and the temperature rises
4° F. or more. This infusion is then
ued until the fever begins to fall,
roughly twice the number of organ-
are added to another intravenous
to boost the temperature back to its
r level. With this double clysis pro-
cedure, at least 6 hours of fever over 103° F. can be obtained in 1 day with relative ease, a third clysis being only occasionally necessary. The next fever treatment, usually given 2 days later, is begun with an infusion containing about 1½ times the number of organisms used in the clysis preceding it, and the double clysis method is again used to sustain the temperature level. This simple procedure is repeated on alternate days, increasing the number of organisms with each new clysis, until the patient has had the total number of hours of fever. If more than two clyses are required in 1 day, the subsequent infusions should consist of distilled water and glucose rather than saline.

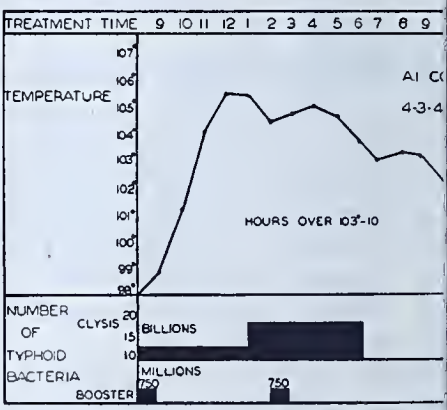
The exact amount of vaccine necessary to produce satisfactory hyperpyrexia cannot be stated, since each patient's tolerance for the protein differs. Occasionally the patient is very sensitive and the total number of fever hours can be obtained with relatively few typhoid organisms. The average patient, however, develops a moderate tolerance for the protein and by the termination of treatment about fifty billion organisms are necessary to produce a good febrile response. The course of fever therapy in such a patient is illustrated in figure 2.

A few patients are more resistant to the vaccine, and at times as many as two hundred fifty billion organisms are required to obtain an adequate temperature rise. When such large quantities are used, there may be undesirable side effects, such as severe headache and muscular soreness. We have attempted to obviate this situation by a combination of the clysis and single-dose method. As is illustrated in figure 3, a single injection is given at the onset of each infusion to shorten the period before the chill. Additional single injections are given intravenously during the febrile period to supplement the clysis and to boost a falling temperature. Such "booster" doses should be relatively small and consist of not more than one-tenth of the number of organisms contained in the clysis. They should not be given while the temperature is rising, as an excessive febrile reaction may occur. The use of multiple









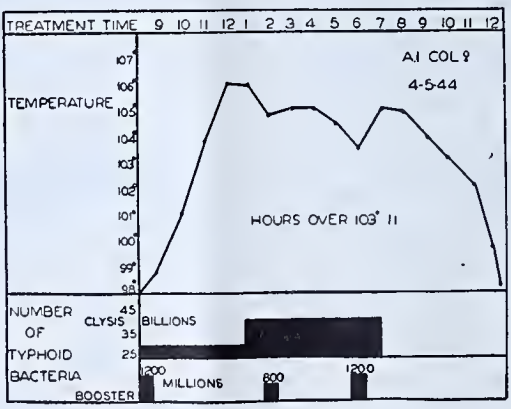


FIGURE 3.—Reproduction of temperature charts showing results of clysis method supplemented by multiple injections of typhoid organisms.

injections of vaccine to supplement
lysis is somewhat dangerous and
be used only by those experienced
safer technic.

our various attempts to produce
yrexia with typhoid vaccine, we have
truck by the quantities of the foreign
1 that may be given without ill ef-
We believe there is a considerable
n of safety in this form of pyreto-
y, dependent, of course, on the use
dually increasing doses of the vac-
build up the patient's tolerance. We
lso been impressed by the ease with
patients tolerate long sessions of
the actual chill is the greatest source
omfort. For this reason we have re-
been inclined to prolong the daily
s of fever, usually up to 10 hours,
reducing the number of treatments
ary and shortening the hospitaliza-
eriod of the patient.

patient's temperature is taken every
nutes and the blood pressure is de-
ed at frequent intervals during the
of treatment. Water is allowed
only in small quantities. Although
is offered throughout the day, it is
y refused. Supplementary feedings
lvisable, however, to avoid excessive
t loss. Blankets and rubber sheets
aced under and over the patient. The
a cradle, as suggested by Knight
workers (*3*), has been found to be
desirable when the patient is rest-
ncooperative, or complains of the ex-
weight of his covers. At the onset
e episode of fever he is given
barbital, chloral hydrate, or paralde-
Codeine is beneficial in relieving
he, muscular soreness, and backache.

ESULTS IN THE TREATMENT OF NEUROSYPHILIS

results cannot be conclusively evalu-
as we have been using the typhoid
e infusion method of fever therapy
ss than 2 years, but a preliminary
of the patients treated has shown
ethod to be therapeutically valuable.
the exception of those cases with
nerve damage, the routine treatment
following fever has been 20 injections of tryparsamide. We have used this relatively short course of chemotherapy because the value of prolonged tryparsamide treatment after fever has been questioned (*8*). Recently, as has been suggested, we have begun the administration of mapharsen at the height of the fever with no aftertreatment (*8*).

Of our 25 patients with paresis treated by the above technic, only 2 are known to have had an unsatisfactory outcome. One patient did well at first but relapsed a year later, while the other has never shown much improvement. Eleven of the cases have had a complete remission and have returned to their former socioeconomic status. In 6 cases insufficient time has elapsed for evaluation, while 4 have been lost in follow-up. In those patients with clinical remission, there has been a corresponding change of spinal fluid with decreased cells and protein. Admittedly, most of our cases of paresis are mild, there being no facilities in the hospital for the care of the more deteriorated paretic patients. In some of the more severe cases, however, remarkable improvement in both neurologic and mental status has been noted immediately following fever treatment.

Of 4 cases of juvenile paresis, improvement has occurred in 3, but the results are much less spectacular than in acquired paresis. The patients with congenital paresis still show considerable evidence of mental deterioration.

We have treated 16 patients with group III asymptomatic neurosyphilis, but insufficient time has elapsed for a complete evaluation. In 5 cases, spinal fluid examination 6 months after termination of treatment showed inactivity of the infection according to the standards outlined by Dattner (*8*).

Of 5 cases of optic atrophy, 2 have become completely blind, while the others have retained the same degree of vision. Because of the great variability of prognosis of this condition, and because of the extensive visual damage (less than 20/70) prior to fever, no definite conclusion can be drawn from this small series. The same

consideration applies to our results in tabes and meningovascular syphilis.

COMPLICATIONS OF FEVER FROM INTRAVENOUS TYPHOID INFUSION

In our series there have been no deaths and, except for 2 instances of excessive temperature response, no serious reactions have occurred. We have observed no evidence of circulatory collapse, although occasionally a mild fall of blood pressure will occur toward the end of the day's treatment. In 2 cases the temperature rose to 108° F., but it fell quickly with cessation of the clysis, removal of the blankets, and tepid sponging. These patients became delirious but there were no serious sequelae. This complication can usually be avoided by careful nursing and constant observation of the patient.

The usual reactions incurred were mild and consisted chiefly of headache, muscular soreness, and cubital phlebitis; none of these were ever serious enough to discontinue treatment. Herpes labialis was noted frequently. Anemia developed occasionally during the course of treatment, and the hemoglobin level fell as much as 6 gm. Most patients lost from 6 to 10 pounds in weight. One case of jaundice occurred, and occasionally edema was noted in a comatose patient. With the appearance of these latter complications, treatment was discontinued. Two patients could not complete the course of fever because of a lack of suitable veins, while 2 others became resistant to the vaccine and malarial fever had to be substituted. After completion of the course of fever, several patients returned to the clinic with mild pedal edema, similar to that noted after malaria (*9*). With rest and a high protein diet this soon cleared up. Although some effort was made to select our cases by excluding those with cachexia, congestive failure, cirrhosis of the liver, and chronic nephritis, we have nevertheless given fever successfully to patients with moderate hypertension, diabetes, peptic ulcer, and obesity. We have chosen 60 as the upper age limit in our cases, but the average age of our patients has been from 40 to 50 years.

DISCUSSION

The infusion method of typhoid therapy has almost entirely supplant use of malarial fever in the treatm neurosyphilis at Grady Hospital. T mainly due to our large Negro p tion, which made necessary the quartan malaria with its associated veniences of a prolonged incubation uncertainty of response, and longe pitalization. Moreover, the maintena a strain of malaria, either tertian or tan, in a general hospital has been to be a troublesome procedure. T vaccine, on the other hand, is ge available and convenient, and in m stances produces satisfactory fever technic of administration by the i method is easily learned and with experience can be managed entirely intern staff. It has also been found t practical procedure in private ho where several of the local physician adopted the method. In contrast to m it permits the use of concurrent ar and bismuth preparations whic thought to have greater effectivenes ing fever than afterwards. For a g hospital, where most neurosyphilis s in the early stage, typhoid vaccine distinct advantages. It seems to be fective for early cases as artificial m of fever induction and at the same t better tolerated and less dangerous. also less expensive than hyperthern inets and 1 nurse may care simultan for as many as 4 patients.

SUMMARY

1. Sixty cases of neurosyphilis hav treated with hyperpyrexia produced continuous infusion of typhoid vac

2. Satisfactory fever can easily b tained by this method with relative fort to the patient and without s complications.

3. A preliminary survey of the peutic results shows a satisfactory re in early paresis and in asympt neurosyphilis.

4. The advantages of this meth hyperpyrexia over malaria for use

neral hospital include shorter hospitalition, greater convenience, ease of administration, and control of temperature. For e Negro, especially, the avoidance of the ng incubation period and uncertainty of sponse of quartan malarial infection ake the use of the continuous infusion ethod of typhoid vaccine a preferable urce of fever therapy.

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The Prevention of Immediate Nausea and Vomiting Following the Administration of Arsenicals Intravenously in the Treatment of Syphilis

Harold W. Seff, M.D.

During an experience with several hundreds of patients being treated for syphilis was noted that many individuals complained of nausea and vomiting immediately after their intravenous injection of eoarsphenamine. Many continued to have his complaint even after oxyphenarsine as substituted for neoarsphenamine. The ausea and vomiting were severe enough n many cases to cause the patients to discontinue treatment.

The reacting patients were questioned egarding their symptoms, and all stated hat the nausea and vomiting were caused y the odor and taste of the drug which as noticed immediately at the start of the jection and before it was completed. In n attempt to counteract this, such measres were tried as chewing gum, smoking cigarette, pinching the nostrils together, melling perfume during the injection, and bstaining from food 2 hours before the injection. None of these procedures proved effective.

It was then decided that temporary anesthesia of the taste buds on the tongue might, by abolishing the taste sensation, prevent reflex nausea and vomiting. To accomplish this, the patient was given, immediately before the intravenous injection, 2 tablets containing ethylaminobenzoate (anesthesine), ¼ gr. each, with instructions to place both tablets upon the tongue and to keep them there until they were dissolved. As soon as this occurred the patient was sent to the treatment room to receive the intravenous injection.

In no instance in which this treatment was used did the patient experience nausea and vomiting. All those previously experiencing these symptoms who received the tablets in the experimental study refused to take subsequent treatments without first obtaining the tablets. Several hundred patients have now been so treated, and in no case has nausea and vomiting occurred.

Health Commissioner, Delaware City-County Department of Health, Delaware, Ohio.

DIAGNOSIS

Serologic aspects of early syphilis. R. C. Arnold and Margaret R. Zwally. New York State J. Med., New York, 44: 2584–2587, Dec. 1944.

This paper discusses the typical and atypical reactivity patterns which are observed in the various stages of syphilis during the use of batteries of serodiagnostic tests.

The type and number of serologic tests selected for use in a given laboratory will vary according to the equipment of the laboratory and the specific clinical program in which the results are to be used. A limited serologic routine will furnish sufficient data for the usual diagnostic purposes and for the evaluation of clinical response to an established treatment. If limited serodiagnostic services are used, however, it must be realized that certain syphilitic serums will escape detection and that the serologic reports may not be in complete agreement with the reports from another laboratory using different test procedures. The quantitative tests are especially valuable in gaging serologic response, as they indicate the decreasing titer or the development of a serologic relapse, while at the same time the qualitative tests give only an unvarying positive report. The reports obtained from a battery of different tests furnish essential data which can be correlated with that secured from observation of the patient's clinical status and therapeutic response to give a complete picture of a case.

Syphilis of the mouth with a brief description of some of the more common diseases which simulate syphilis of the mouth. Charles C. Wilson, William B. Dunning and Howard Fox. Ann. Dent., Baltimore, 3: 39–63, Sept. 1944.

This paper discusses in some detail the differential diagnosis of the various forms of syphilis of the mouth and points out that it is the responsibility of the dentist to discover oral manifestations of systen diseases.

The serodiagnostic tests are briefly di cussed. Conditions affecting lesions of t oral mucosa are mentioned: their situati in a moist medium, the presence of vario bacteria, the use of artificial dentures, t ingestion of excessively hot and sha foods, the use of tobacco, and the occu rence of injuries from malocclusion.

The oral lesions of primary, secondai and late syphilis, acquired and congenit are described, including those of li tongue, oral cavity, teeth, and palate.

Precautions against infection of t nurse or physician attending a patient wi infectious syphilis are suggested, and it pointed out that dentists should treat su a patient only if he is receiving adequa antisyphilitic therapy. Elective den treatment should be postponed until t infective stage of syphilis is passed.

The common nonsyphilitic diseas which may simulate syphilis are describ and the means of differentiating them a reviewed. Included in this discussion a aphthous stomatitis, herpes simplex, herp zoster, pemphigus, erythema multiforn lichen planus, lupus erythematosus, leuk plakia, lupus vulgaris, Vincent's infecti granuloma pyogenicum, epithelioma, ling plicata, lingua geographica, dysvitaminos hypovitaminosis, avitaminosis, pellag fungus infections, and perleche.

Effect of malaria on serologic tests f syphilis. Arthur A. Rosenberg. Bu U. S. Army M. Dept., Carlisle Ba racks, No. 84: 74–80, Jan. 1945.

This study was undertaken for the pu pose of determining which of the serolo tests for syphilis gave the least proporti of falsely positive reactions in malaria a whether it was possible to distinguish m laria from syphilis on the basis of defin patterns of positivity among the differe tests.

The tests employed were the standa flocculation tests described by Kahn, Ma zini, Eagle, Hinton, and Kline and t standard complement fixation test of K mer. The antigens in all cases were a proved by the originators of the test.

The cases were classified into 4 groups depending on the species of plasmodia found in the blood smear: falciparium, vivax, falciparum and vivax (when both were present), and not classified (when the parasite density was low).

More than 8,000 serologic tests were performed on individuals whose histories were negative for syphilitic infection. Observations of various clinical manifestations were made, and correlations between these and the responses to the tests are reported. A characteristic pattern of positivity was found in most malarial serums.

These are the author's conclusions: (1) The Hinton flocculation test for syphilis yielded the smallest proportion of falsely positive reactions in malaria of any of the serologic technics employed. (2) The pattern of positivity in malaria, that is, positive Kahn and Mazzini tests, doubtful Kolmer and Kline tests, and negative Eagle and Hinton tests, can usually be differentiated from that of syphilis. In the absence of continued evidence of malarial infection, persistence of positive reactions to any serologic test beyond 6 weeks should arouse the suspicion of syphilis.

Late secondary syphilis (?) (Papillomatous papules of the lower lip; ulcerated gumma of the left inguinal area). A. Benson Cannon. Arch. Dermat. & Syph., Chicago, **50**: 230, Sept. 1944.

A 34-year-old Negro was seen at the Vanderbilt Clinic on Nov. 12, 1943, complaining of a bubo of 3 weeks' duration in the left inguinal area. The lesion had broken down 3 days before.

Examination showed a large ulceration, measuring 2x1 cm. and about 1.5 cm. deep, in the left inguinal area; the base was granulating and the borders were sharp. There was no genital lesion. Shotty right inguinal nodes and enlarged epitrochlear nodes were present. Raised, confluent, papillomatous, infiltrated plaque-like lesions appeared on the lower lip. In both angles of the mouth, there were moist split papules.

The Frei test (left arm) on November 15 and repeated on November 22 was negative. The Ducrey reaction (right arm) tested on the same dates was also negative. Both the Wassermann reaction of the blood and the Kline reaction were 4 plus. Three darkfield examinations of lesions on the lip were negative for spirochetes.

After 2 injections of a bismuth preparation and 4 days of iodide medication, the lesions in the angle of the mouth disappeared; the lesions of the lower lip definitely decreased. The bubo was cleaner, although not decreased in size.

The author states that he was not certain that the ulcer in the groin was a broken-down lymph node.

Granuloma venereum. (Granuloma venereo.) E. E. Tello and J. A. Herrero. Rev. argent. dermatosif., **28**: 79–88, 1944.

During the years 1941 and 1942 a total of 31 cases of granuloma inguinale was reported in the province of Cordoba. The authors present an additional case which was observed in a 23-year-old Argentinian. He gave a history of gonorrhea at 22 years which had been treated and cured. In February 1940 he noticed a small, painless tumor in the left inguinal region which during the course of 15 days increased to hen-egg size, at which stage it was painful and inflamed. He was hospitalized and the lesion was removed surgically. Although cicatrization followed this procedure another ulceration appeared in the left genitocrural fold 2 weeks later and a lesion on the dorsum of the penis after another 20 days; finally, destructive lesions appeared on the prepuce and spread to the glans penis. The ulcerations showed a tendency to progression and hypertrophy. The centers of the ulcers were flat and the borders raised and vegetating. There was an associated bilateral inguinal adenopathy. The purulent secretion covering the lesions was found to be bacteriologically negative; neither Koch nor Ducrey bacilli were found. Blood serologic reactions for syphilis were negative. A biopsy of the border of one of the lesions was made. The epidermis showed the phenomenon of papillomatosis; there were small abscesses

containing polymorphonuclear neutrophils, eosinophils, and some mononuclear cells. The dermis showed foci of infiltration of plasma cells, neutrophils, some eosinophils and Donovan bodies. Treatment with a sulfonamide drug and later with tartar emetic resulted in some improvement of the lesions.

TREATMENT

The chemotherapy of syphilis. Joseph Earle Moore. Bull. New York Acad. Med., New York, 21: 3–17, Jan. 1945.

The history of the chemotherapy of syphilis, which covers 451 years, from 1493 to the present, may be divided into 3 periods, the first from 1493 to 1903, the second from 1903 to 1943, and the third from June 1943 to the present. The author summarizes the events of the first, notes the accomplishments and confusions of the second, and outlines in some detail the developments of the third.

Throughout all 3 periods, the problem of time-dose relationship has been constantly present, regardless of what chemotherapeutic agent was being used, but not until the late 1920's was any organized effort made to solve it. Then, the League of Nations and the Cooperative Clinical Group undertook a systematic study of the results of the various schedules of treatment. The effects of prolonged arsenical-bismuth treatment are now fairly well known, as are the immediate results of the more intensive methods. The late results of the intensive methods will not be available for another generation.

In June 1943, Mahoney, Arnold, and Harris demonstrated that penicillin was effective in early syphilis in rabbit and in man. Because of the importance of the control of the disease in conserving manpower in wartime, an organized investigation of the uses of the drug was begun with the cooperation of the military and governmental agencies and civilian clinics and laboratories.

Preliminary results of these studies permit certain general statements concernin the treatment of syphilis with penicillin:

1. Multiple injections are required fc the treatment of early syphilis.

2. The intramuscular route of admir istration is satisfactory; intrathecal injec tions are not necessary in neurosyphili and probably not in late neurosyphilis.

3. The optimum interval between ir jections is 3 to 6 hours.

4. Total doses of 60,000 to 1,200,00 units administered at 3-hour intervals da and night for 7½ days give practicall identical immediate results.

5. The relapse rate is in inverse rati to the total dosage, 60,000 units giving ap proximately 100 percent relapse; a dose c 1,200,000 units giving a relapse rate of onl 15 to 20 percent.

6. The rate of relapse in a very larg dose (2,400,000 units) seems less frequen but data are insufficient to furnish proof.

7. Reducing the duration of treatmer by half is not helpful.

8. Lengthening the interval between in jections to 12 hours is unsatisfactory, bu whether there is any material differenc between the 3- and the 6-hour interval i undetermined.

9. Penicillin in combination with an ar senoxide may be more effective than eithe drug alone.

10. Penicillin is apparently effective i early syphilis treatment resistant to arseni and bismuth, in the prevention of con genital syphilis in infants born of recentl infected mothers, in early neurosyphilis, i infantile congenital syphilis, and in re lapsed patients.

11. Four dose schedules are under tria for use in neurosyphilis, the phase of lat syphilis most studied so far.

12. A trend toward seroreversal of th blood test following the use of penicilli in late syphilis is evident.

13. Reactions from penicillin are negli gible except for the Jarisch-Herxheimer re action.

A method for use in ambulatory patient is essential, since the present minimum re quirement of 10 days' hospitalization pose an economic problem.

The history of the treatment of syphilis during the past 450 years indicates the desirability of the continuation of an organized, nation-wide, governmentally sponsored study of the problem.

Intensive treatment of early syphilis—method of Eagle and Hogan. George Miller MacKee and Girsch D. Astrachan. New York State J. Med., New York, 44: 2577-2584, Dec. 1944.

The authors report their observations on 61 patients with syphilis treated by the Eagle and Hogan method.

The effect of the treatment on the visible lesions and the serologic reactions of patients are discussed, and case reports are given. The reactions occurring are described, and a comparison of the percentage of reactions in this series with that in a series of patients treated by the intravenous drip method is made.

The authors state the following conclusions:

1. The method of Eagle and Hogan appears to be an efficacious method of antisyphilitic therapy.
2. It causes fewer reactions than the intravenous drip method.
3. It is still in the experimental stage, and it should be used cautiously, preferably under the supervision of a trained syphilologist.
4. This method may be employed when dealing with cooperative and careful patients.

Successful treatment of gonorrhea with a single intramuscular injection. Henry Welch, Lawrence E. Putnam, William A. Randall and Robert P. Herwick. J.A.M.A., Chicago, 126: 1024, Dec. 16, 1944.

In order to determine the effect of penicillin X on the gonococcus, a study was made of the results of the treatment of 68 patients with gonorrhea with a single intramuscular injection of 25,000 units of this substance. Most of the 68 patients, 35 of whom were males and 33 females, were sulfonamide resistant. The criterion of cure used in most instances was 3 negative cultures obtained 1, 3, and 5 days after treatment had been completed. Sixty-four (94 percent) patients were cured. For comparative purposes, a group of 58 patients with gonorrhea, 31 males and 27 females, were treated with a single intramuscular injection of 25,000 units of commercial penicillin. Using the same criterion, 37 (64 percent) of those treated were cured. Three of the patients who failed to respond favorably to the commercial penicillin treatment were cured by a subsequent treatment with a single injection of 25,000 units of penicillin X.

Studies of the blood concentration were made on 7 patients treated with penicillin X and on 8 patients treated with commercial penicillin. These concentrations were determined with the serial dilution technic using Bacillus subtilis as the test organism, ½, 1, and 2 hours following intramuscular injection. During the first 2 hours after treatment a consistently higher concentration of penicillin X was maintained in the blood. Urinary excretion studies were made over a period of 8 hours on 9 patients, 4 being treated with penicillin X and 5 with commercial penicillin. During the first 2-hour period, 58 percent of the penicillin X injected was excreted, as compared with 68 percent of the commercial penicillin. After 8 hours, the total excretion of penicillin X was 71 percent as compared with 80 percent of commercial penicillin.

The chemotherapy of gonorrhea. J. F. Mahoney and C. J. Van Slyke. Bull. New York Acad. Med., New York, 21: 18–26, Jan. 1945.

The authors discuss the various systems of the chemotherapy of gonorrhea used in the history of that disease from the standpoint of their efficacy both as curative and as preventive agents, and attempt an estimate of the future of the disease and its control.

The various sulfonamides and the theories of their mode of action are outlined. Reasons advanced for the failure of these drugs in a certain percentage of patients treated are (a) the chance encountering of a strain of Neisseria gonorrhoeae whose biology differed from

the average to the extent of being resistant naturally to chemotherapy and (b) the deficiency or absence in certain patients of some host factor which is essential to the effective action of the compound. Concerning the first of the these, the paper refers to an unpublished study and the conclusion to which it points: strains of the N. gonorrhoeae seem to have the ability to retain their respective susceptible or resistant characteristics. The second concept, that involving host factors, is dismissed for lack of exact information.

The rate of sulfonamide cure under hospital conditions is given as approximately 80 percent.

Concerning the incidence of gonorrhea, the authors say the peacetime level is not known and is not likely to be known in the future. During the last war, it increased, but during the present conflict, the anticipated increases in the rates of infection do not as yet appear to have taken place. Military reports for personnel within continental United States set the present rate at about 30 per 1,000 for all venereal diseases, with gonorrhea contributing about two-thirds of the total.

The impetus which the discovery of penicillin has given to investigative work in the field of antibiotics is discussed.

Various schedules for the use of penicillin in checking gonococcic infections are mentioned, and reference is made to a recent report by Sternberg and Turner of the pooled experiences of a group of clinicians in the cure of about 1,800 patients.

Some alarm has recently been expressed as to the dangerous possibilities in the future role of gonorrhea, including the production of symptomless carrier states and drug resistant strains which will move unchecked through a population group in the proportion of an epidemic. The present authors do not agree with this opinion, nor do they suggest that eradication of the disease is within the range of possibility. They believe the disease will probably always be with the human race, but that through the wise application of the knowledge now available, its ill effects may be reduced to a minimum. They conclude that if the incidence of gonorrhea can be held at its present level for the duration of the war, it can be considerably reduced when peace returns great numbers of people to a more rational mode of existence. Then, with the aid of penicillin therapy, combined health forces should be able to reduce the disease to a point where it will no longer be important either as a source of ill health to the human race or as a health problem to the public.

The use of procaine hydrochloride with the intramuscular administration of penicillin sodium. William F. Shannon and E. L. Zielinski. Mil. Surgeon, Washington, 95: 501, Dec. 1944.

The authors present a method of using procaine with penicillin in order to prevent the occurrence of pain and spasm which sometimes follow the intramuscular injection of that solution.

The usual dosage of 100,000 units of penicillin was dissolved in 20 cc. of normal saline. This was divided into 5 doses of 4 cc. each, and to each dose was added ¼ cc. of 2 percent procaine hydrochloride. In vitro tests showed no reduction in the potency of penicillin following the addition of procaine, and clinical trial on 100 patients confirmed that finding. The patients so treated were considerably more comfortable than those given penicillin without the procaine.

Penicillin in sulfonamide-resistant gonorrhea. John G. Menville and Clarence W. Ross. U. S. Nav. M. Bull., Washington, 43: 997–1000, Nov. 1944.

The authors report the results in the penicillin treatment of 144 patients with sulfonamide resistant gonorrhea. This series may be compared with a previous series of 124 cases reported in September 1944.

All the patients were apparently cured. The uncomplicated cases, 115 (99.1 percent) in number, responded to 1 dose of 100,000 units of penicillin given intramuscularly; the complicated cases received concomitant intramuscular and intravenous injections totaling 300,000 units daily until cured. One patient with gonorrheal arthritis was treated with simultaneous injec-

tions of penicillin into the joint, muscle, and vein. Three cases of latent infections, all of which were in patients with complications, occurred following penicillin therapy. One patient developed epididymitis after receiving 100,000 units of penicillin intramuscularly, indicating that the gonococcus was not eradicated by the use of the drug. Subsequent intensive continuous penicillin therapy for 5 days did not shorten the course of the epididymitis.

Chemotherapy, pyrotherapy and penicillin in the treatment of gonorrhea. Davis H. Pardoll and Robert L. Dennis. U. S. Nav. M. Bull., Washington, 43: 988–996, Nov. 1944.

This paper reports observations made on 166 patients with gonorrhea treated by means of chemotherapy, pyrotherapy, and penicillin. It was found that less than 50 percent of the patients treated with chemotherapy responded favorably. Pyrotherapy produced favorable responses in 74 percent of those resistant to sulfonamides, and penicillin apparently cured all patients on whom it was used.

The authors express the opinion that gonorrhea is showing a definite increase in its resistance to treatment with sulfonamides, that the previously accepted dosage of both sulfadiazine and sulfathiazole is inadequate, and that pyrotherapy is a valuable adjunct in the management of sulfonamide resistant gonorrhea. They report 100 percent of cures in the penicillin treatment of 89 patients with gonorrhea, 66 of whom were sulfonamide resistant and 7 of whom had failed to respond to pyrotherapy.

Gonorrheal ophthalmia. Malcolm E. Miller. J. Indiana M. A., Indianapolis, 37: 679–681, Dec. 1944.

The author reports a case of gonorrheal ophthalmia treated with penicillin.

A male patient, aged 16 years, was admitted to the hospital 10 days after possible exposure to gonorrheal infection, complaining of profuse discharge and pain in the right eye. Examination showed marked edema of both lids of the affected eye and an extremely profuse, purulent exudate from the conjunctival sac, as well as a thin, purulent, penile discharge. Cultures and spreads were positive for the gonococcus.

Besides other local therapy to the involved eye, penicillin ophthalmic ointment was instilled in the conjunctival sac every 2 hours, and 100,000 units of penicillin were given intramuscularly daily for 8 days. The purulent exudate was markedly decreased within 48 hours and completely eliminated within 5 days. An opacity involving the lower half of the cornea appeared the second day after admission to the hospital, the central portion of which developed into an ulcer. This appeared to have healed completely within 2 weeks leaving some residual scarring but causing only slight interference with vision. An eye culture on the eighth day of hospitalization was negative, as was each succeeding culture. There was 20/20 vision in the affected eye at the close of treatment.

The author comments that until more experience is gained, the favorable results in this case must be accepted with caution.

Bismuth stomatitis during the treatment of syphilis in the Army. Sidney S. Silverman. Mil. Surgeon, Washington, 95: 486–489, Dec. 1944.

Dental examination of approximately 500 men receiving bismuth treatment for syphilis revealed that 70 percent of them had some gingival manifestation of bismuth stomatitis and that the condition appeared chiefly in those patients who failed to practice oral hygiene. The bluish-black line appears first at the site of a preexisting inflammation of the gingival tissues. The standard dose of 0.2 gm. of bismuth will cause little or no deposit of pigment where the oral hygiene is good, whereas in a mouth that lacks proper care, the same dosage will give a heavy line and its concomitant symptoms.

The author comments that all patients about to undergo bismuth antisyphilitic treatment should have a dental examination and instruction in oral hygiene, followed by periodic checking particularly midway in the course of treatment, since the line of pigmentation usually appears

between the seventh and ninth injections. Training film 8-155 is mentioned as being an effective means of teaching proper care of gums and teeth.

Hazards of hypertherm treatment. John Wallace and S. R. M. Bushby. Lancet, London, 2: 459–464, Oct. 7, 1944.

The authors report the results of clinical observations of 254 patients with resistant gonorrhea who underwent hypertherm treatment at 106.6°F, for 8 hours. Detailed clinical, hematologic, and biochemical investigations were made in 37 of these cases.

The complication most commonly seen was anoxia with bilirubinemia which developed into clinical jaundice in 37 cases. Hippuric acid tests showed a considerable reduction of liver function. Oxygen and carbon dioxide therapy lessened anoxia, reduced vomiting, and appeared to prevent circulatory collapse. Hypertherm treatment caused a transient polymorphleukocytosis and a transient hemodilution. There was a small transient rise in nonprotein nitrogen, and a tendency for plasma chlorides and urinary chlorides to fall. Premedication with 6 gm. of sulfathiazole did not increase the hazards of hypertherm treatment.

Renal tubular degeneration due to sulfonamide drugs. Anna M. Young. Urol. & Cutan. Rev., West Palm Beach, 48: 531–536, Nov. 1944.

This paper discusses the findings at autopsy of 4 cases of renal degeneration following the use of sulfonamide drugs. In two of the cases, the patients died in uremia due to a necrotizing nephrosis; in the third case, the cause of death was apparently parenchymatous damage to the liver as well as to the kidneys; in the fourth, the cause of death was generalized peritonitis and the kidneys showed reversible degenerative changes with repair of the renal lesions.

The author comments that the necrotizing nephrosis seen in these cases was similar to that seen in bichloride of mercury poisoning, and agrees with the comment of Hellwig and Reed, which she quotes as follows: "The histological findings in our case are not in accord with the belief of most clinicians that renal failure after sulfadiazine therapy is caused by mechanical blocking of the urinary passages and not by actual tissue damage due to the toxicity of the drug. In our case the most striking alterations were present in the convoluted tubules."

The doses of sulfonamides administered in these cases were well within the therapeutic range. There was no consistent premonitory change either clinically or in the laboratory findings. In each of the 3 cases terminating in uremia, administration of the drug was stopped and therapy was resumed later either with the same or with another drug of the sulfonamide group. The author believes it possible, as has been suggested by Davidson and Bullowa and by Stiles, that sensitization and/or hypersensitivity to the drug plays a role in the production of the harmful effects of its administration.

LABORATORY RESEARCH

The anti-spirochetal activity of penicillin in experimental infections. N. Ercoli and Lillian C. Lafferty. Proc. Soc. Exper. Biol. & Med., Utica, 57: 4–6, Oct. 1944.

This paper reports the results of an investigation made for the purpose of determining the minimal healing and sterilizing doses for penicillin in experimental spirochetal infections.

Rabbits infected 8 weeks previously with Treponema pallidum showing orchitis of both testicles besides chancriform lesions containing large numbers of spirochetes were given intravenous injections of varying doses of penicillin. The potency of the drug used as determined in the cup test varied between 100 and 300 units/mg. Three rabbits received 4 to 6 intravenous injections of single doses ranging from

33,000 to 47,000 units/kg.; three received 4 injections with single doses of 7,500-10,000 units/kg., and two received 4 injections with single doses of 3,800-4,300 units/kg.

Mice infected intra-abdominally with a suspension of mouse blood containing spirochetes of relapsing fever (Borrelia novyi) were treated subcutaneously with penicillin using single doses ranging from 5,000 units/kg., to 50,000 units/kg.

The following results were stated:

1. The single intravenous dose of penicillin sodium salt required to produce disappearance of T. pallidum in experimental rabbit syphilis is 33,000-47,000 units/kg. The same effect can be obtained with about 16,000 units/kg. if the drug is administered repeatedly over a period of 72 hours in doses of approximately 4,000 units/kg. The latter dose was found sufficient to produce healing of primary lesions in 10 to 15 days.

2. The minimal effective dose of penicillin sodium salt in Borrelia novyi infections of mice was found to be 25,000 units/kg. mouse; doses of 200,000 units/kg. and more might be considered as curative.

3. The lymph nodes of 4 rabbits treated with the highest doses of penicillin used, 132,000-282,000 units/kg., transferred into testicles of healthy animals, produced a syphilitic infection, indicating that even the high doses of penicillin were not sufficient to sterilize the animals.

Biologic false positive serologic tests for syphilis. Bernard D. Davis. Medicine, Baltimore, 23: 359–414, Dec. 1944.

This paper reviews the literature for the years 1930-1943. The author summarizes the available information concerning the incidence of false positive tests and discusses the laboratory differentiation of false positive serums and the clinical diagnosis of false positive reactions.

The serologic tests for syphilis are subject to marked variations in sensitivity; these account for a large proportion of the discrepancies in published reports on the incidence of biologic false positive reactions in various diseases. Many of the cases reported have undoubtedly been technical false positives based on unreliable earlier Wassermann tests. Evaluation surveys have improved the performance of the laboratories, but fluctuation in results on weakly positive serums is inevitable.

The incidence of transient positive tests following acute infections depends largely on the frequency of testing during the acute and convalescent stages. Although postinfectious and postvaccinial positive reactions occasionally last as long as 3 months, most become negative within a few days or weeks. Since it is customary to perform serologic tests on hospital patients only on admission, before the acute infection has fully developed its antibodies, it is likely that the ability of many common infections to lead to false positive serologic tests is grossly underestimated. Those causes of transient positive reactions (malaria and vaccination) which have been tested at short intervals have shown some degree of reaction in nearly 100 percent of the cases, but the majority of these were only 1 or 2 plus reactions, ordinarily reported as negative or doubtful.

False positive serologic tests are common in leprosy, malaria, infectious mononucleosis, vaccination against smallpox, ratbite fever, relapsing fever, lupus erythematosus, and possibly atypical pneumonia. There is no reliable evidence that the tests are affected by pregnancy, menstruation, scarlet fever, jaundice, subacute bacterial endocarditis, tuberculosis, or hyperproteinemia. Inadequate data are available on measles, mumps, infectious hepatitis, lymphogranuloma venereum, and chancroid.

Transient false positive reactions may occur in apparently normal individuals without recent illness and in cases of some diseases the incidence of which is so low as to suggest that the relationship may be coincidental. It has recently been suggested that even persistently positive reactions may occur in nonsyphilitic patients. In widespread serologic surveys the number of innocent victims may be large.

Since low titer syphilitic serums may show discrepancies between the results obtained with various test antigens and fluctuation in apparent reactivity of successive serums, these are not adequate

criteria for considering a positive serum false.

The various complement fixation and flocculation tests for syphilis are antigen-antibody reactions. The lipid antigen is widely distributed in human and other mammalian tissues, and is an effective antigen for forming antibodies if mixed with a foreign protein before inoculation. It is not clear whether the Wassermann antibody is formed in response to Wassermann antigen from the organisms or to tissue antigen rendered active by the spirochete. If the latter hypothesis is correct, no difference would be expected to exist between the Wassermann antibodies in syphilis and in other diseases.

Some of the false positive reactions may be eliminated in the future by purification and improvement in specificity of lipid antigens of the Wassermann group, but there is no reason to expect all false Wassermann antibodies to differ in any given respect from the true antibody. Attempts to find consistent empirical physicochemical differences between syphilitic and false positive serums have thus far failed. To the reviewer the most promising approach to the problem is the detection of antibodies to antigens of the spirochete other than Wassermann antigen.

Measures are recommended for the handling of seropositive cases which have no clinical basis for diagnosing syphilis. The most important procedure in all cases except that of pregnancy is observation without treatment during a probationary period of 3 months. During that period, many false positive tests will be revealed as transient, but there is no verification test to help in the diagnosis of those which remain positive.

PUBLIC HEALTH ADMINISTRATION

Venereal disease rates overseas. Bull. U. S. Army M. Dept., Carlisle Barracks, No. 83: 16-18, Dec. 1944.

The rates of venereal disease infection among Army personnel in various areas overseas, both white and Negro, since December 1943 are given. In December 1943, the total rate was about 50 per 1,000, and this figure declined to about 35 per 1,000 in May 1944.

The North African theater had an abnormally high rate concomitant with the invasion of Italy. The Middle East and the Persian Gulf Command have had consistently higher than the average rates for all troops overseas. The Caribbean area has made consistent progress, reaching a low of about 30 per 1,000 although the rate of infection among native population and native troops is high. The rate in Panama is comparable to that in the United States. The Southwest Pacific area has a low rate of infection, which declined still further during 1944. In the Asiatic theater, the rate has fluctuated from about 70 to 40 per 1,000. The rate in the British Isles has steadily declined to a low of about 23 per 1,000. The situation in France is potentially dangerous, but efforts have been made to forestall repetition of the Italian experience.

In most theaters of operation, the incidence of syphilis and gonorrhea among Negro troops overseas is much higher than that among white troops.

Venereal disease control in Nova Scotia. Eldon L. Eagles. Nova Scotia M. Bull., Halifax, 23: 240–245, Sept. 1944.

This paper was presented at the annual meeting of the Medical Society of Nova Scotia in July 1944.

According to information given out by the Armed Forces Medical Services of Canada, in the 3½-year period—Jan. 1, 1940 to June 30, 1943—there were recorded 35,036 venereal infections in the Armed Forces. The treatment of these infections required nearly 700,000 hospital days and the loss of nearly 700,000 training days. The cost of medical care and lost training time amounted to nearly $8,000,000. There were enough man-days lost in the Air Force to man an air squadron for a year, in the Army to fight Canada's share of the Sicily battle, and in the Navy enough to escort 8 convoys across the Atlantic. The

uation among the military personnel is reflection of that existing in the civilian pulation.

The infection rate among Army personnel stationed in Prince Edward Island d Nova Scotia (M.D. No. 6) is slightly low the average rate for all of Canada; e rate among R.C.A.F. personnel, staoned in the Eastern Air Command, is ell above the average.

For the year ending Nov. 30, 1943, 133 ases of syphilis and 241 cases of gonorrhea ere reported to local health officers by hysicians for all of Nova Scotia. In the ape Breton Island Health Unit, out of 456 blood samples donated to the Red ross Blood Donor's Clinic, the Kahn eactions in 33 were positive for syphilis, n incidence rate of 9.5 per 1,000.

The control of venereal disease must epend on systematized social action. An mendment to the Public Health Act requires that venereal diseases be reported o the Minister of Health. Free drugs and linics, as well as free diagnostic laboratory service through the Public Health aboratories, are included in Nova Scotia's rogram of venereal disease control.

The program of the department of health or the control of venereal disease cannot succeed without the support of the medical profession; control begins with the practicing physician.

Uniform standards of penicillin. Medical News. J.A.M.A., Chicago, 126: 1097, Dec. 23, 1944.

International agreement concerning a uniform standard and unit of penicillin has been reached by the health committee of the League of Nations, according to an announcement on October 20 by Sir Henry Dale, president of the Royal Society, London. The British Medical Journal pointed out that the new international standard penicillin would be finally purified and crystallized in the United States, but the material for this purpose would be freely supplied by manufacturers in both Great Britain and the United States, and added that there is no substance in the talk about trade rings in the manufacture of penicillin.

The importance of a knowledge of sexual habits in the diagnosis and control of venereal disease, with special referenee to homosexual behavior. Josephine Hinrichsen. Urol. & Cutan. Rev., St. Louis, 48: 469–486, Oct. 1944.

Effective control of venereal diseases demands a knowledge of all sources of infection. Since human sexual habits are unpredictable, some infections are overlooked and become hidden sources for the spread of these diseases.

This paper discusses the role of unusual modes of sexual intercourse in the transmission of venereal diseases and the characteristics of various types of venereal disease infection of the mouth and throat, of the anus and rectum, and correlates these with the mode of infection. Those phases of the problem of homosexuality which have a direct bearing on the diagnosis of venereal disease and the tracing of sources of infection are presented.

The author concludes that the classification "extragenital chancre" should be discarded because (1) the classification is too vague; one interested in anal chancres has to look through many references on extragenital chancre, most of which do not include anal chancres, and (2) the classification is useless and misleading, since many of the so-called extragenital areas of the body play a role of genital organs in "perverted" sexual contact and become infected in the same way as the genital organs. A chancre of the mouth contracted through fellatio is not adequately classified by the term, "extragenital." Primary lesions of syphilis, therefore, should be classified according to their exact location, and whenever possible, the manner of infection should be specified.

More knowledge of unusual types of sexual behavior, including overt homosexuality among both men and women and more complete examination of patients based on such knowledge is essential to the success of the venereal disease control program. In the interest of public welfare, physicians should overcome their reluctance to study the problem and report their findings.

New Cases of Syphilis and Gonorrhea in States, Territories, and Possessions

Health officers' monthly statement: Reported for the first 5 months of fiscal years 1944-45 and 1943-44

Area	Cases of syphilis and gonorrhea reported for first 5 months of fiscal years below:											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44
Total† United States	[1]142,097	[1]193,714	[1]29,384	[1]31,749	[1]38,377	[1]50,795	[1]58,798	[1]84,072	4,496	[1]5,674	[1]112,368	[1]125,2
Alabama	5,816	7,236	816	1,106	1,272	1,701	1,211	1,774	132	172	2,632	2,9
Arizona	799	1,230	237	282	244	327	240	464	67	56	475	7
Arkansas	3,799	3,809	837	502	1,191	1,281	1,390	1,369	107	90	2,535	2,0
California	11,932	13,198	2,129	2,158	2,646	3,130	6,599	7,220	368	411	13,510	13,4
Colorado	1,164	1,874	316	431	359	530	447	841	42	72	1,009	1,4
Connecticut	(*)	1,296	(*)	150	(*)	495	(*)	379	(*)	67	(*)	6
Delaware	284	396	62	44	88	92	109	61	10	7	96	
Dist. Columbia	354	3,456	44	442	68	847	141	1,995	11	59	289	1,5
Florida	6,751	13,080	849	1,370	2,406	3,888	2,908	6,024	182	257	5,893	7,3
Georgia	4,614	7,437	1,236	1,387	1,859	3,062	1,361	2,755	158	229	3,291	4,9
Idaho	394	249	71	123	92	48	210	57	15	4	207	3
Illinois	9,464	11,683	1,571	1,447	2,227	2,822	5,385	7,166	281	248	8,919	9,8
Indiana	2,500	3,775	525	531	313	354	858	1,388	94	111	1,245	1,4
Iowa	676	1,011	147	210	192	254	282	431	31	79	1,056	7
Kansas	1,139	1,094	292	201	193	224	605	625	49	44	1,215	8
Kentucky	2,272	3,328	546	456	527	737	850	1,424	123	134	2,032	1,5
Louisiana	5,149	8,506	1,168	1,277	1,539	2,108	1,251	2,242	207	193	5,278	5,6
Maine	366	332	74	72	46	37	147	171	28	30	765	5
Maryland	3,466	7,271	743	710	859	719	862	1,122	77	54	1,995	3,7
Massachusetts	1,788	2,260	451	494	(§)	(§)	1,232	1,647	105	119	1,891	2,1
Michigan	7,432	7,644	1,283	1,052	2,068	1,963	2,725	3,244	190	203	5,188	4,8
Minnesota	916	1,080	146	98	83	106	632	797	33	51	1,048	8
Mississippi	8,841	11,111	3,020	3,823	2,475	3,058	2,832	3,759	514	470	13,087	12,6
Missouri	3,919	4,166	866	756	1,064	1,035	1,727	1,948	131	139	3,390	2,3
Montana	183	174	40	50	19	21	47	74	5	4	134	1
Nebraska	(*)	527	(*)	87	(*)	293	(*)	109	(*)	19	(*)	7
Nevada	167	354	45	10	1	57	65	256	7	13	286	1
New Hampshire	117	88	8	11	9	28	87	43	11	3	67	
New Jersey	3,410	4,906	525	581	916	1,571	1,773	2,554	150	192	2,121	2,3
New Mexico	712	840	145	187	193	184	335	422	53	47	563	6
New York	12,935	15,869	2,573	2,358	2,612	2,669	7,273	10,215	345	449	5,978	8,2
North Carolina	(*)	4,757	(*)	1,256	(*)	1,883	(*)	1,527	(*)	91	(*)	3,5
North Dakota	90	137	18	47	13	22	36	49	6	7	154	1
Ohio	8,252	10,031	1,726	1,461	2,286	2,379	3,873	5,008	367	402	3,006	2,1
Oklahoma	2,889	3,415	462	456	770	997	941	1,221	106	131	3,196	2,1
Oregon	836	898	221	255	95	67	482	552	33	24	1,005	
Pennsylvania	4,793	5,819	876	741	1,528	2,274	1,559	2,151	183	299	0	
Rhode Island	360	435	89	30	31	42	167	318	17	10	690	
South Carolina	3,666	7,032	1,001	1,459	1,228	2,964	1,151	2,298	141	169	3,012	2,3
South Dakota	168	204	26	47	54	31	65	89	21	16	210	
Tennessee	5,978	7,835	934	1,089	2,313	3,227	2,377	3,266	182	167	4,951	6,1
Texas	6,232	9,563	1,287	1,276	2,144	2,758	2,198	3,595	231	258	4,074	4,3
Utah	253	425	81	107	21	61	147	250	4	7	245	
Vermont	77	120	8	37	24	37	33	42	7	4	180	
Virginia	3,952	6,192	1,181	1,893	1,595	2,322	1,032	1,736	92	122	2,273	5,3
Washington	1,637	1,835	344	354	380	454	651	763	32	56	2,092	3,3
West Virginia	832	1,650	267	272	114	224	163	334	18	47	999	1,3
Wisconsin	(*)	420	(*)	84	(*)	(*)	(*)	332	(*)	4	(*)	
Wyoming	723	666	98	56	220	83	339	312	30	15	86	
Territories, Possessions and Canal Zone												
Alaska	(*)	37	(*)	24	(*)	6	(*)	3	(*)	1	(*)	
Canal Zone	395	(*)	54	(*)	76	(*)	217	(*)	15	(*)	214	(*
Hawaii	(*)	354	(*)	67	(*)	51	(*)	216	(*)	19	(*)	
Puerto Rico	(*)	7,757	(*)	747	(*)	1,573	(*)	2,527	(*)	940	(*)	1,3
Virgin Islands	103	91	16	18	69	52	11	15	2	6	39	
Actual total‡ U. S. and Possessions	142,595	208,953	29,454	34,182	38,522	55,148	59,026	89,180	5,013	6,821	112,621	133,3

*No data available.
**Includes "not stated."
†Based on States reporting in both fiscal periods.
‡Includes all reported cases.
§Included in late latent.
[1]Based on 45 States.

New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over

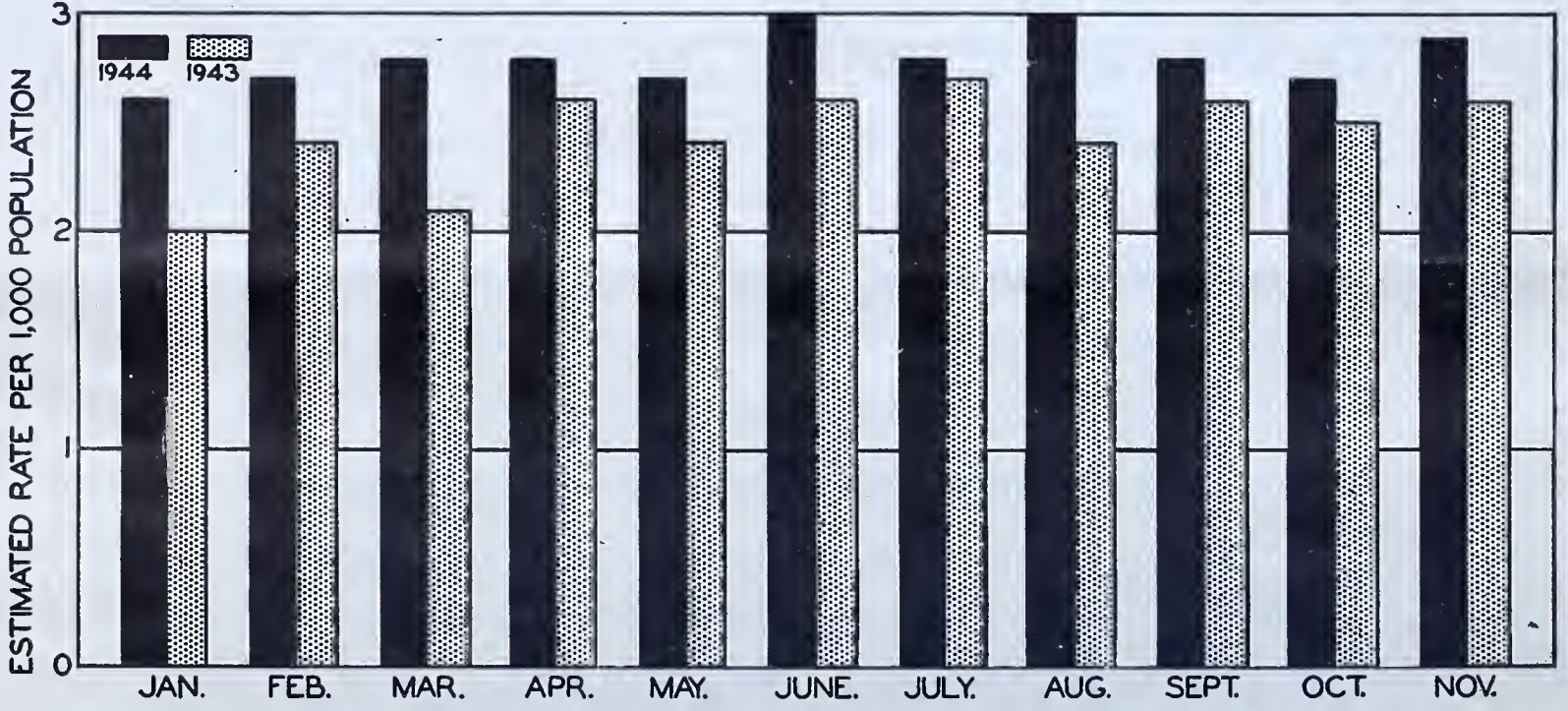
Health officers' monthly statement: Reported for the first 5 months of fiscal years 1944-45 and 1943-44

City	Cases of syphilis and gonorrhea reported for first 5 months of fiscal years below:											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44
Total†	[1]53,303	[1]73,042	[2]10,515	[2]8,334	[2]12,322	[2]15,575	[2]24,145	[2]32,187	[2]1,310	[2]1,333	[1]37,328	[1]33,457
kron	434	406	111	55	89	102	204	230	30	19	267	139
lanta	1,147	1,344	318	324	319	399	490	609	20	14	1,390	525
ltimore	2,332	5,909	622	541	592	508	732	858	34	32	1,212	1,398
rmingham	1,297	2,220	160	136	336	615	329	516	34	39	248	272
ston	677	766	166	164	80	0	337	487	28	14	680	578
ffalo	760	830	121	82	110	117	505	609	24	22	450	384
icago	6,427	5,898	1,144	936	1,597	1,457	3,523	3,374	163	131	6,004	5,255
ncinnati	1,024	1,443	174	187	(§)	(§)	850	1,256	0	0	448	456
eveland	1,802	1,759	369	322	581	576	809	818	43	43	791	616
lumbus	609	656	181	121	139	133	268	363	21	19	209	135
allas	851	1,040	204	204	240	211	401	616	6	9	364	329
ayton	451	871	51	94	165	241	221	506	14	30	250	291
enver	536	899	152	179	176	230	174	352	17	25	477	755
etroit	4,138	5,278	784	635	1,446	1,632	1,825	2,917	83	94	2,357	2,545
onolulu	106	212	29	37	13	33	57	127	4	15	458	486
ouston	(*)	799	(*)	130	(*)	282	(*)	356	(*)	31	(*)	976
dianapolis	718	947	151	282	85	9	181	211	8	12	197	42
rsey City	151	247	21	25	48	50	74	166	8	16	38	20
ansas City	593	774	116	128	133	156	300	487	25	31	446	408
s Angeles	4,666	4,742	1,323	0	399	1,848	2,798	2,756	146	138	2,893	2,043
uisville	551	1,045	170	135	114	190	229	445	17	11	631	376
emphis	2,541	2,777	324	250	1,220	1,330	904	1,166	93	31	2,129	2,589
ilwaukee	231	196	43	24	0	0	184	158	5	1	191	97
inneapolis	259	296	72	50	38	47	141	192	8	5	466	358
ewark	723	983	149	116	236	255	329	589	19	23	532	396
ew Orleans	646	1,299	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	950	820
ew York	9,124	10,918	2,078	1,900	2,225	2,407	4,517	6,226	226	276	5,978	5,767
akland	681	697	94	80	148	168	358	428	18	15	742	577
klahoma City	(*)	1,001	(*)	99	(*)	271	(*)	300	(*)	15	(*)	414
maha	233	239	43	17	51	160	132	47	7	15	200	215
iladelphia	2,482	4,816	331	151	448	614	588	620	63	52	413	388
ttsburgh	669	3,586	104	(*)	177	(*)	348	(*)	40	(*)	124	23
rtland	365	407	132	95	41	27	187	284	5	1	694	407
ovidence	171	214	18	45	20	13	93	138	7	4	64	69
chester	126	107	27	20	8	9	90	75	1	3	183	120
. Louis	2,507	2,384	509	344	774	816	1,148	1,140	76	74	1,753	705
. Paul	96	132	16	17	20	24	51	81	2	3	122	139
n Antonio	(*)	503	(*)	54	(*)	132	(*)	297	(*)	18	(*)	591
n Diego	543	574	76	46	161	167	240	335	26	19	506	392
n Francisco	1,128	1,236	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,126	885
attle	654	568	146	67	162	112	331	353	8	9	794	689
racuse	269	451	21	14	12	17	233	406	3	14	181	130
oledo	231	420	25	69	28	85	171	251	7	15	81	52
ashington, D. C.	354	3,456	44	442	68	847	141	1,995	11	59	289	1,586
ctual total‡	53,303	75,345	10,619	8,617	12,499	16,260	24,493	33,140	1,350	1,397	37,328	35,438

*Data not available.
**Includes "not stated."
†Based on cities reporting in both fiscal periods.
‡Includes all reported cases.
§Included in late latent.

[1]Based on 41 cities.
[2]Based on 38 cities.

ANNUAL GONORRHEA CASE RATES
IN CITIES OF 200.000 POPULATION AND OVER
BASED ON PROVISIONAL MONTHLY DATA, 1944 AND 1943



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Serologic Survey and Venereal Disease Educational Program at the San Francisco County Jail

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and

Lee Hand, M.D.[2]

A review of the literature shows that investigators recognize the unfortunate lack of adequate venereal disease control programs in penal institutions (*1, 2, 3, 4*). It is frequently difficult to secure adequate audiences at public health venereal disease lectures and often these lectures are directed to women's clubs and service groups who are at an older age level and are not likely to be exposed to, or to contract a venereal disease. The prison group, however, represents a population with a high potential venereal disease exposure rate and one that is likely to contribute markedly to the dissemination of these diseases. It is unfortunate that this group has not been more adequately reached in the past. It is important, in the interest of venereal disease control, that the group be more extensively reached in the future.

Considerable progress has been made in providing serologic examinations and treatment facilities for inmates of State penal institutions during the past 10 years (*1, 2, 3, 5, 6*). This progress apparently has not been matched in county penal institutions as we have found no reports in the literature in the past 10 years regarding such institutions. From the viewpoint of social value, it would seem relatively more important to develop such programs in county institutions than in State institutions because the average length of confinement in State institutions is for a term of years, while that in county institutions is for a period of only 3 to 6 months. The Department of Commerce, Bureau of the Census, reports the median length of sentence for 1940 in State penal institutions as 5.8 years and time served as 20.5 months; in Federal penal institutions the median length of sentence was less than 2 years and time served 11.9 months (*7*). The latest available figures for penal institutions under county or municipal jurisdiction are for 1933 and show a median length of sentence of 35.7 days and time served as 16.9 days (*8*).

Serologic examinations and the initiation of antisyphilitic treatment on any group of people is of small value unless accompanied by an educational program of sufficient merit to develop in those examined an understanding of the problems of venereal disease. It was noted in the present series that as many as 22.5 percent of the total examined did not know the result of their previous blood test. The value of such an educational program in a penal institution together with a procedure for directing released inmates to clinics where their treatment will be continued has been recognized by others (*1*).

In 1941 and 1942 the San Francisco County Jail had a yearly average of 6,300 new admissions of which 89.8 percent were men and 10.2 percent were women. The average daily population during this period was 660. The average sentence served was from 3 to 4 months.

Prior to 1940 routine serologic examinations were not performed on inmates and only those who requested it received antisyphilitic treatment. Late in 1940 a routine serologic examination program was established and inmates having a sentence of 1 month or longer were examined. In each case, a medical history was secured which included information regarding previous serologic examinations, history of syphilis and gonorrhea, and history of previous treatment. This history and the result of the serologic examination offer pertinent

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TABLE 1.—*Positive serologic reactions found on routine examination of 3,908 individuals admitted to the San Francisco Jail during 1940 and 1941, by race and age*

Age at time of examination (in years)	Race											
	White			Negro			Other			Total		
	Total examined	Number positive	Percent positive	Total examined	Number positive	Percent positive	Total examined	Number positive	Percent positive	Total examined	Number positive	Percent positive
10–19	36	2	5.6	7	0	0.0	5	0	0.0	48	2	4.2
20–29	411	31	7.5	101	34	33.7	43	5	11.6	555	70	12.6
30–39	921	78	8.5	91	30	33.0	97	21	21.7	1,109	129	11.6
40–49	1,201	95	7.9	52	11	21.2	75	20	26.7	1,328	126	9.5
50–59	710	60	8.5	16	2	12.5	26	5	19.2	752	67	8.9
60–69	99	9	9.1	3	0	0.0	1	1	100.0	103	10	9.7
70–79	3	0	0.0	0	0	0.0	0	0	0.0	3	0	0.0
Unspecified	5	0	0.0	2	0	0.0	3	0	0.0	10	0	0.0
Total	3,386	275	8.1	272	77	28.3	250	52	20.8	3,908	404	10.3

TABLE 2.—*Positive serologic reactions found on routine examination of 3,908 individuals admitted to the San Francisco Jail during 1940 and 1941, by race and marital status*

Marital status	Race											
	White			Negro			Other			Total		
	Total examined	Number positive	Percent positive	Total examined	Number positive	Percent positive	Total examined	Number positive	Percent positive	Total examined	Number positive	Percent positive
Single	1,838	129	7.0	148	36	24.3	140	28	20.0	2,126	193	9.1
Married	499	35	7.0	61	17	27.9	74	15	20.3	634	67	10.6
Widowed	168	25	14.9	14	4	28.6	10	4	40.0	192	33	17.2
Divorced	566	42	7.4	17	9	52.9	10	2	20.0	593	53	8.9
Separated	274	18	6.6	27	7	25.9	13	3	23.1	314	28	8.9
Unspecified	41	26	63.4	5	4	80.0	3	0	0.0	49	30	61.2
Total	3,386	275	8.1	272	77	28.3	250	52	20.8	3,908	404	10.3

TABLE 3.—*Positive serologic reactions found on routine examination of 3,908 individuals admitted to the San Francisco Jail during 1940 and 1941, by sex and marital status*

Marital status	Sex											
	Male			Female			Sex unspecified			Total		
	Total examined	Number positive	Percent positive	Total examined	Number positive	Percent positive	Total examined	Number positive	Percent positive	Total examined	Number positive	Percent positive
Single	2,089	179	8.6	37	14	37.8	0	0	0.0	2,126	193	9.1
Married	559	55	9.8	73	12	16.4	2	0	0.0	634	67	10.6
Widowed	164	25	15.2	27	8	29.6	1	0	0.0	192	33	17.2
Divorced	544	39	7.2	49	14	28.6	0	0	0.0	593	53	8.9
Separated	271	16	5.9	43	12	27.9	0	0	0.0	314	28	8.9
Unspecified	46	30	65.2	3	0	0.0	0	0	0.0	49	30	61.2
Total	3,673	344	9.4	232	60	25.9	3	0	0.0	3,908	404	10.3

statistical information regarding a population of this type.

All blood specimens were tested in the San Francisco Health Department Laboratory by the screen Mazzini test with Kahn and Kolmer tests being done on specimens showing any degree of positivity. The social record was taken by a lay representative of the health department and clerical work was performed by inmates who had had clerical experience. The social record was taken under conditions that afforded as much privacy as possible, a room having been set aside at the jail for the exclusive use of those concerned with the survey. A second serologic examination was performed on all those having an initially positive serologic reaction. No diagnosis of syphilis was made until at least 2 positive serologic examinations taken on different days were secured. All persons found to have syphilis were referred to the jail physician for antisyphilitic treatment, if indicated, during their confinement. Upon release from custody, each inmate found to have syphilis was given a travel record and requested to report to the San Francisco City Venereal Disease Clinic for continuation of treatment or observation.

Each inmate was encouraged to ask questions regarding the purpose of the blood test and the significance of the results. An educational program consisting of the showing of a venereal disease motion picture and a venereal disease lecture on a personalized basis was presented monthly. Although attendance was voluntary, at least 90 percent of the jail population attended these programs. A question period was provided at the conclusion of each lecture. The audience usually asked pertinent questions which were answered quite frankly by the speaker. Opportunity was also afforded for questions of a more personal nature which were answered privately. Venereal disease literature was distributed on request.

STATISTICAL ANALYSIS

A total of 3,908 prisoners was examined in 1941 and 1942, of whom 404 (10.3 percent), were found to have positive serologic reactions. These results compare closely with those reported by Stanley (*9*) who found 9.2 percent of 10,000 prisoners at San Quentin, California State Prison, to have positive serologic reactions, and with those of Jones (*10*) who reported 10.3 percent positive serologic reactions at the Washington State Penitentiary, 11.0 percent at the McNeil Federal Penitentiary, and 7.6 percent at the Washington State Reformatory. They are higher than those reported by Münsterer (*11*), who found 8.0 percent positive serologic reactions in prisoners at the Bavarian penal institutions. Our findings for prison inmates were lower than many reports in the literature. Heller (*12*) reported 29.3 percent positive reactions in Tennessee; Hawk (*13*) 21.7 percent positive in Fort Leavenworth, Kansas; Huntley (*14*) 12 percent positive in southern Michigan; Arvidson (*2*) 14 percent positive in Minnesota; Simons (*15*) 24.1 percent positive in South Carolina, and Lorenz (*16*) 12.5 percent positive in Wisconsin. It should be noted that reports of high prevalence came from southern penal institutions with a high Negro population.

The incidence of positive serologic tests in the 3,908 prisoners on the bases of age and race is shown in table 1. It will be noted that the occurrence of positive tests was approximately constant for all age groups containing significantly large numbers of persons examined. Differences between the age groups are well within the limits of chance variation. These findings agree with the reports of Münsterer (*11*), Heller (*12*), and Simons (*15*).

Table 2 shows the distribution of positive serologic reactions on the bases of marital status and race. The widowed have a higher incidence than other marital groups, except in the Negro race where the divorced rate exceeded all others. We have found no other report on a similar population of penal institutions which includes a complete marital status breakdown. It is of interest to note in table 3, which analyzes the incidence of positive serologic reactions by marital status and sex, that the incidence in the male group

TABLE 4.—*Positive serologic reactions found on routine examination of 3,908 individuals admitted to the San Francisco Jail during 1940 and 1941, by race and sex*

Sex	Race											
	White			Negro			Other			Total		
	Total examined	Number positive	Percent positive	Total examined	Number positive	Percent positive	Total examined	Number positive	Percent positive	Total examined	Number positive	Percent positive
Male	3,187	230	7.2	244	64	26.2	242	50	20.7	3,673	344	9.4
Female	196	45	23.0	28	13	46.4	8	2	25.0	232	60	25.9
Unspecified	3	0	0.0	0	0	0.0	0	0	0.0	3	0	0.0
Total	3,386	275	8.1	272	77	28.3	250	52	20.8	3,908	404	10.3

was highest among the widowers, while in the female group the highest incidence was found among the single women. In the male group, those divorced and separated show a relatively low incidence as compared with the widowers; in the female group, those widowed, divorced, and separated are consistently high.

A labor union serologic survey (*17*) of the San Francisco area showed a high incidence of positive serologic reactions in the widowed and divorced groups, while we noted the highest incidence in the widowed group of our jail population.

A sex comparison, presented in table 4, shows the female prisoner to have a much higher incidence than the male. This has also been the finding of Münsterer (*11*). An analysis by sex and race shows this higher incidence in the female is not due to differences in racial composition, but is consistent within the white and Negro races. The white male group showed an incidence of 7.2 percent, a statistically significant difference from the 20.3 percent for the white female group. Because of the comparatively small number of Negroes examined, a statistically significant difference cannot be determined. However, the difference between the Negro sexes was considerable; the Negro male showed an incidence of 26.2 percent and the Negro female 46.4 percent. Our finding of a high incidence of positive serologic reactions in the female is in agreement with the findings of other penal institutions for women (*18, 19*). The probable reasons for this are that many of the women prisoners are prostitutes and in women, criminality is much more frequently connected with sex delinquency than in men.

Of the prisoners examined 437 (11.2 percent), as shown in table 5, gave a previous

TABLE 5.—*Results of serologic tests for syphilis made on 3,908 individuals admitted to the San Francisco Jail during 1940 and 1941 giving history of previous knowledge of syphilis and/or gonorrhea*

Serologic reaction on admission	History of venereal disease					
	Total examined		Syphilis		Gonorrhea	
	Number	Percent	Number	Percent	Number	Percent
Positive	404	100.0	221	54.7	72	17.8
Negative	3,504	100.0	216	6.2	753	21.5
Total	3,908	100.0	437	11.2	825	21.1

istory of syphilis and 825 (21.1 percent) ave a previous history of gonorrhea. Over alf (54.7 percent) of those having posi- ive serologic reactions gave a history of revious knowledge of the disease. Six ercent of those having negative tests also ave a history of infection. We found table 6) that while only 6.4 percent of he total prisoners examined had never iad a previous blood test, 22.5 percent did iot know the result of their previous blood ests. Of those having positive serologic reactions, 34.6 percent reported that their previous tests were negative.

The public health activity of the community is reflected in the figures of tables 7 and 8. It is observed that 49.2 percent of those found to have positive serologic reactions upon routine examination at the jail had been under diagnostic study for syphilis during the year previous to admittance. Further, 53.7 percent had at some time in their lives received injection treatment for syphilis.

TABLE 6.—*Results of recent previous serologic tests made on 3,908 individuals examined for syphilis on admission to the San Francisco Jail during 1940 and 1941*

Serologic reaction on admission	Result of recent previous test									
	Positive		Negative		No data		No test		Total	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Positive....	95	23.5	140	34.6	136	33.7	33	8.2	404	100.0
Negative...	27	0.8	2,518	71.9	743	21.2	216	6.1	3,504	100.0
Total.	122	3.1	2,658	68.0	879	22.5	249	6.4	3,908	100.0

TABLE 7.—*Number of individuals who had been under study for syphilis during the year preceding admission to and examination at the San Francisco Jail during 1940 and 1941*

Serologic reaction on admission	Under study		Not under study		No data		Total	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Positive.....	199	49.2	199	49.2	6	1.5	404	100.0
Negative.....	1,298	37.0	2,189	62.5	17	0.5	3,504	100.0
Total.....	1,497	38.3	2,388	61.1	23	0.6	3,908	100.0

TABLE 8.—*Number of individuals who had been under treatment for syphilis at some time before admission to and examination at the San Francisco Jail during 1940 and 1941*

Serologic reaction on admission	Under treatment		Not under treatment		No data		Total	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Positive.....	217	53.7	185	45.8	2	0.5	404	100.0
Negative.....	211	6.0	3,271	93.4	22	0.6	3,504	100.0
Total.....	428	11.0	3,456	88.4	24	0.6	3,908	100.0

DISCUSSION

A review of the literature reveals a lack of adequate venereal disease control programs in penal institutions under county and municipal jurisdiction. It is important that this group be reached more extensively in the future since it represents a population with a high potential venereal disease exposure rate. It is relatively easy to introduce such a program in county penal institutions. They are generally located in close proximity to municipalities, and existing facilities of jurisdictional health departments with the assistance of prisoner clerical workers are usually adequate to provide such service.

The value of such a survey is shown in the high percentage of positive serologic reactions and the amount of previously untreated syphilis discovered. An analysis of table 5 shows that 45 percent of those who had positive serologic reactions disclaimed any past knowledge of syphilis. In addition, infected prisoners who previously knew of their infection were offered antisyphilitic treatment. In the past, prisoners knowing of their infections often did not receive treatment while in custody either because such treatment was not available or because the prisoner was not interested in treatment, usually because of his lack of adequate appreciation of the importance of such treatment (*4, 5*).

The discovery of these infected persons is also of community social benefit. Approximately 44 percent of the inmates examined were under 40 years of age. In the same age group, we found 50 percent of the total infections. (Table 1).

There are numerous plans and recommendations in the literature for conducting an educational and case-finding venereal disease program in State penal institutions. It remains the responsibility of the local public health venereal disease workers to join with the penal institution authorities to institute an adequate local program. As mentioned earlier, it seems of considerable importance to reach the inmates of county penal institutions who are numerically greater than those in State institutions and who reenter society after only a short sojourn in these institutions.

CONCLUSIONS

1. A serologic survey and an educational program in a county penal institution are described.

2. Of 3,908 persons examined 404 (10.3 percent) were found to have positive serologic reactions for syphilis.

3. The incidence of positive serologic reactions by age, sex, race, and marital status is given and discussed.

4. Present positive serologic reactions are compared with a past history of syphilis; only 54.7 percent of those with positive serologic reactions admitted previous knowledge of syphilis.

5. Such a program is of public health value both to the community and to the individual.

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A State-wide Gonococcus Culture Service
A System Utilizing the Mail for Transmission of Specimens

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Gonorrhea case finding has long been handicapped by the inadequacy of the available laboratory methods of diagnosis. The smear method is neither highly specific nor sufficiently sensitive. The culture method, although perfectly specific when properly performed, and considerably more sensitive, presents technical difficulties which have limited its use mostly to large hospitals and health centers where the specimens can be taken promptly to the laboratory. Culture service could not be generally available without a satisfactory method of mailing specimens. Some years ago, therefore, Bergsma and Stein of this bureau developed a method (*1*) using horse plasma-hemoglobin agar slants by which 156 positive cultures were obtained from mailed specimens taken from patients whose concurrently prepared smears yielded only 71 positives. On the basis of this success, it was decided to set up an experimental program on a State-wide basis. This was done, and in February 1943 the service was announced in the Journal of the Medical Society of New Jersey (*2*). In addition it was brought to the attention of physicians in the State by other means of publicity and promoted by public health nurses and other public health workers.

Central laboratories and culture stations were set up. The former prepare the media, assemble the mailing outfits, carry out the subculturing and identification of gonococci, and report the results to the participating physicians and clinics. The culture stations distribute containers, receive the specimens, incubate them for 18 to 24 hours at 37°C., and forward them to the central laboratories. The culture stations are located in hospitals, local health departments, and institutions.

MATERIALS AND PROCEDURES

Mailing outfits consist of tubed slants of horse plasma-hemoglobin agar, each individually packed in a metal container (5½" x1" I.D.) which in turn is fitted into a cardboard mailing container (6"x1¼" I.D.) bearing a self-addressed label and a 3-cent postage stamp. Use of the inner metal container is necessary to comply with

[1]Surgeon, U. S. Public Health Service.

postal regulations. A sterile applicator swab and a data slip with a complete set of directions printed on its reverse side are also included in each outfit. The directions warn against leaving the swab in the tube, gouging the slant, and tipping the tube (danger of spilling carbon dioxide). The physician is instructed to deliver the specimen to the incubator at the culture station within three hours after streaking it. The screw-top of every outfit bears a label with a date of expiration stamped thereon.

The culture medium used is the Peizer-Steffen modification of horse plasma-hemoglobin agar (*3*) dispensed in Wassermann-type test tubes (4″x⅜″ I.D.) in quantities of 2 to 3 cc. per tube. Slants are made with a fairly deep butt (½ inch thick) at the bottom of the tube. This supporting butt proves essential in preventing sagging and other types of distortion of the slant during the course of its subsequent handling. The slants are hardened in the refrigerator, after which most of the air in each tube is replaced by gaseous carbon dioxide. Experiments have shown that the medium remains usable for at least 6 weeks after its date of preparation.

When received at the central laboratory all mailed specimens are routinely separated into 3 categories on the basis of the degree of bacterial growth present on the slants. Group 1 includes all slants possessing no growth of any kind; group 2 is made up of slants showing moderate amounts of growth which consists, to some degree, of well defined, isolated colonies. Group 3 is composed of slants whose colonies are either densely intermingled or are overgrown (wholly or partially) by spreading colonies of contaminating organisms.

Treatment of group 1.—Slants in this group are given additional overnight incubation at 36° C., and then reexamined. Those which remain sterile are reported as negative. Slants which show growth after the additional incubation period are reclassified and placed in either group 2 or group 3, depending on the degree of this resultant growth.

Treatment of group 2.—Colonies possessing the colonial morphology typical of the gonococcus are picked from the slant's surface with a sterile platinum needle and transferred to a tube containing about 0.2 cc. of sterile broth dilution medium containing 2 percent proteose peptone no. 3 (Difco) and 0.4 percent sodium chloride. The portions of these "fished" colonies which adhere to the slant are flooded with oxidase reagent (p-aminodimethylaniline monohydrochloride) in order to determine their oxidase reaction. These colonial remnants are also examined microscopically. If the suspected colonies are oxidase-positive and are composed of gram-negative diplococci, a loopful of the broth suspension is streaked on a plate of horse plasma-hemoglobin agar and incubated for 48 hours at 35° to 36° C., in an atmosphere containing carbon dioxide (10 percent). If, on the other hand, inspection of the slant reveals no colonies morphologically typical of those of the gonococcus, a few drops of oxidase reagent are allowed to trickle down the surface of the slant. Colonies which exhibit oxidase-positivity are fished off while still viable (in the "pink-phase" of the characteristic pink-to-black series of color transitions) and transferred to a tube of sterile broth dilution medium. If the microscopic examination of a representative loopful of this suspension discloses the presence of gram-negative diplococci, subcultures are prepared in the manner described above. Following incubation, group 2 plates are examined for colonies which (1) possess the colonial morphology typical of the gonococcus, (2) are oxidase-positive, (3) are composed of gram-negative diplococci, and (4) ferment only dextrose when inoculated into sugar media (sucrose, maltose, and dextrose) and allowed to incubate for 24 hours at 36° C. Only those plates possessing colonies which satisfy all 4 of these conditions are reported as positive.

Treatment of group 3.—The dense growth on the surface of these slants makes visual detection of typical gonococcus colonies impossible. Therefore, the slants are flooded with a few drops of oxidase reagent and colonies which turn pink

are immediately picked off and transferred to a tube of sterile broth dilution medium. A loopful of this suspension is routinely subjected to microscopic examination. If the presence of gram-negative diplococci is thus established, subculturing procedures are carried out. Successful recovery of the gonococcus is defined by the same criteria, which hold for the group 2 plates.

In the event that the subcultures fail to produce any oxidase-positive colonies composed of gram-negative diplococci, the specimen is reported as "suspicious" and an explanation is typewritten on the reverse side of the report form. For example, in picking suspected colonies from the specimen slants of group 3, some degree of concomitant contamination is certain to accompany the "fished" material into the tube of broth. If the subcultures prepared from such a specimen produce no oxidase-positive colonies composed of gram-negative diplococci, the report on this "suspicious" specimen will explain: "Although colonies composed of gram-negative diplococci were present on this specimen slant, extensive contamination made it impossible to isolate and establish the identity of these suspicious organisms by means of routine sugar fermentation tests."

Mailed culture results compared with smear results

Mailed culture	Smear*	8/28/42 to 12/31/43		1/1/44 to 10/20/44		Total	
		Number	Percent	Number	Percent	Number	Percent
Positive	Negative	145	41.3	154	58.1	299	48.5
Positive	Positive	147	41.9	84	31.7	231	37.5
Negative	Positive	59	16.8	27	10.2	86	14.0
Positive	Positive or negative	292	83.2	238	89.8	530	86.0
Positive or negative	Positive	206	58.7	111	41.9	317	51.5
Total positive specimen		351	100.0	265	100.0	616	100.0

* All smears were retained for examination by technicians at the specimen sources or laboratories other than ours.

From this table it can be seen that during the entire period the mailed culture plan has been in operation, only 86 (14 percent) of the 616 specimens diagnosed positive failed to be diagnosed by the culture method, whereas 299 (48.5 percent) were missed by the smear examination. This result is even more striking when it is recalled that the culture is 100 percent specific, while false positive smears occur not infrequently.

When reports of the specimens examined in 1942 and 1943 are compared with those examined in 1944 it is seen that the superiority of the culture over the smear was apparently more marked in the later period. This increase in relative efficiency may actually have been due, in part, to a decrease in the efficiency of smear examinations, as might well be expected under wartime conditions which find depleted technical staffs laboring under increased laboratory loads. However, the improvements in technic resulting from the continued practice and experience of handling the slants at both the specimen sources and the central laboratory, undoubtedly contributed significantly to the increased superiority of the mailed culture during the later period studied. This is borne out by the fact that during 1942 and 1943, of 528 specimen slants possessing oxidase-positive colonies composed of gram-negative diplococci, successful subculturing and identification procedures were possible in the case of all but 130 (25 percent), which were reported as "suspicious." In 1944, however, only 92 (19 percent) of 494 specimen slants possessing oxidase-positive colonies composed of gram-negative diplococci, were not successfully subcultured.

CONCLUSION

That this program has demonstrated its value is indicated by its acceptance by physicians and clinics throughout the State. Some military installations have used the

service also. The number of cultures for gonococcus performed by the New Jersey State Department of Health during the past 2 years has increased by more than fourfold, practically all of the rise being in specimens submitted by mail. Currently we are examining specimens at the rate of about 20,000 per year, approximately 13,000 of which are received through the mail.

Physicians who previously did not have access to laboratory facilities have been enthusiastic in praising the service as an aid in case finding. Numerous instances have occurred where repeated smears (as many as 8) were negative and the first culture positive. This is understandable in view of the 1.7 to 1 superiority over smears which is demonstrated by this study. Expressed in another way, this study shows that smears fail to detect gonorrhea almost four times as often as our service. However, in a small proportion of the cases, the mailed culture failed to confirm a positive smear, indicating the need to continue the use of smears along with the cultures.

Physicians are grateful also for the assurance that a positive report can be absolutely relied upon as indicating the presence of gonococci. The reports which were previously available to them (smears) indicated only the presence of an organism resembling the gonococcus in morphology and staining properties.

The present cost of this service (excluding the initial investment for equipment) is about 75 cents per specimen. This cost will decrease as the volume of mailed specimens increases. Unquestionably the service would be less expensive if it were part of a generalized bacteriologic service rather than a specialized one. Also, in computing the cost per specimen it was not possible to separate the cost of research work. If this could be done the rate would be lower.

SUMMARY

1. A practical procedure is described for a State-wide gonococcus culture service with specimens transmitted through the mail to a central laboratory.

2. As a case-finding procedure, the method is more effective than smears. Of 616 positive specimens, only 86 (14 percent) were not detected by the mailed culture method, whereas, 299 (48.5 percent) were missed by the smear examinations.

3. False positive reports are eliminated.

4. In 2 years, the volume of mailed specimens in New Jersey has increased to a rate of about 13,000 per year. The total rate (including delivered specimens) is about 20,000 per year.

5. The cost at present is about 75 cents per specimen. This will decrease as the volume of this service increases, and would be lower if the program were part of a generalized bacteriologic service rather than a specialized one.

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DIAGNOSIS

Quantitative serologic tests for syphilis. Albert Heyman. New England J. Med., Boston, 232: 124–127, Feb. 1, 1945.

The indications for quantitative serologic testing are discussed in this paper, and cases are reported which illustrate how these tests aid in the recognition of certain manifestations occurring in syphilitic infection.

Quantitative testing has been found to be useful in the following instances: (1) the diagnosis of primary syphilis when darkfield examinations of genital lesions are negative, (2) determining the presence

of congenital syphilis in infants and children by means of comparing reagin titers in mother and child, (3) determining early cutaneous relapse, (4) differentiating between seroresistance and serologic relapse, (5) the detection of prozoning, and (6) the detection of biologic false positive reactions.

Case reports are given illustrating the value of quantitative testing in 5 of the conditions named. Frequent reference is made to the literature.

The author is of the opinion that quantitative serologic tests, though indicated only in selected cases, are a valuable tool in the diagnosis and treatment of syphilis.

Verification tests in serodiagnosis of syphilis. Charles R. Rein and George R. Callender. Bull. U. S. Army M. Dept., Carlisle Barracks, No. 85: 108–112, Feb. 1945.

Rein and Callender review the literature and discuss the several methods developed for the differentiation of true and false positive reactions to serologic tests for syphilis. They are of the opinion that the average serologist has not been able to distinguish consistently between true and false positive reactions by the use of any verification test yet devised and that for the present these tests should be considered in the experimental stage and that further investigative work on the subject is necessary. At present, the final diagnosis of a syphilitic infection in doubtful cases should depend on the ensemble of available data, including (1) history, (2) physical examination, (3) radiologic examinations of the heart and aorta, (4) spinal fluid examination, (5) examination of contacts, marital partners, brothers, and sisters, and (6) repeated serologic examinations in the same and other laboratories. Additional laboratory examinations should be made, including blood counts, blood spreads, heterophil antibody tests, sedimentation rates, specific complement-fixation, precipitation and agglutination tests, and albumin-globulin ratio studies, in order to rule out nonsyphilitic diseases which may cause false positive serologic reactions.

The following requirements are set up as criteria of any verification test intended for routine use:

1. Serums from syphilitic individuals with positive serologic tests should always give a syphilitic type of verification reaction.

2. Serums from nonsyphilitic individuals with positive serologic tests should always give the false positive type of verification reaction.

3. The diagnosis of syphilis should be established in persons who consistently give the syphilitic types of verification reaction on repeated examination.

4. The diagnosis of syphilis should be excluded in persons who consistently give the biologic false positive type of verification reaction on repeated examination.

The conclusion is stated that any new verification test should be subjected to critical evaluation by independent workers before it is adopted as a routine procedure for the differentiation between true and false positive serologic reactions.

The slide test for the serological diagnosis of syphilis. J. L. Hamilton-Paterson, W. T. S. Cole and G. L. C. Usher. J. Path. & Bact., Edinburgh, 56: 335–342, July 1944.

Since the variable behavior of the Kahn antigen has been the most serious drawback to the use of the Laughlen slide precipitation test in the diagnosis of syphilis, the authors attempted to find a method for standardizing the antigen.

This paper describes the method and the use of the slide test.

The authors report that on a total of 12,865 serums, the slide test has shown a greater sensitivity (98.68 percent) than the Kahn test or Wassermann reaction taken separately or together. It is less specific than the other two tests. Its reliability combined with its rapidity and simplicity renders it most suitable for the preliminary sorting out of large numbers of serums.

Pseudocarcinomatous hyperplasia in primary, secondary, and tertiary cutaneous syphilis. Herbert Lawrence. Arch. Path., Chicago, 38: 128–131, Sept. 1944.

It is frequently difficult to distinguish histologically between true carcinoma and

the pseudocarcinomatous hyperplasia occurring in primary, secondary, and tertiary cutaneous syphilis. The latter's mimicry of carcinoma of grade 1 or grade 2 frequently is complete and it may even resemble to some extent anaplastic carcinoma. The histologist must consider the diagnosis of pseudocarcinomatous hyperplasia in all lesions of the skin showing epithelial proliferation with invasiveness, and in every such lesion he should use all the additional laboratory and clinical information available.

Extragenital primary syphilis with pseudocarcinomatous hyperplasia occurs frequently at carcinoma-bearing sites, and occasionally a solitary lesion of late secondary syphilis or of precocious benign tertiary syphilis presents the same diagnostic problem. The problem is further complicated by the occasional appearance of a case in which carcinoma becomes superimposed on tertiary cutaneous syphilis.

The clinician should send to the pathologist with the specimen an adequate history of the case and a report of a serologic test for syphilis. Then, in making the final diagnosis, he must correlate the gross appearance of the lesion and the history of the case with the histologic observations.

Lymphogranuloma venereum in pregnancy. William F. Finn. Am. J. Obst. & Gynec., St. Louis, **48:** 696-701, Nov. 1944.

The author describes a rare condition—lymphogranuloma venereum in pregnancy—and reports the results in 11 patients.

The etiology, pathology, and incidence of the disease in its various forms are briefly reviewed. According to this author, the early stages of the disease, other than inguinal adenitis, are rarely treated, since they are rarely recognized. Various therapeutic measures are described.

The salient points in the histories of 10 patients in the present series are summarized, and the eleventh is given in some detail, since it is believed to be the only case of lymphogranuloma venereum associated with rupture of the uterus that has been reported.

Of the 11 patients, 1 was white, 2 were Puerto Rican, and 8 were Negro. Rectal stricture, the most common obstetrical complication of lymphogranuloma venereum, was present in 8 patients. Of these 8 patients, 1 died of arsenical encephalitis in the sixth month of pregnancy, 3 were delivered spontaneously, 3 were delivered by forceps, and in 1, rupture of the uterus occurred, and the fetus, stillborn, was delivered by cesarean section.

Of the 3 patients without stricture, 1 had acute proctitis, 1 fistula-in-ano, and in 1 a positive Frei test was the only evidence of the disease. One patient delivered vaginally had a colostomy of 10 years' standing. In 2 cases of rupture of the rectum, breech extraction was performed.

The author finds that most patients with lymphogranuloma venereum are anemic and syphilitic. Perirectal fibrosis or the presence of soft tissue masses or fixation of the posterior vaginal wall make vaginal delivery difficult and dangerous. With breech presentation in a patient with stricture of the rectum, external cephalic version should be attempted.

Most observers agree that lymphogranuloma venereum is transmitted to the fetus during or after birth, rather than by intrauterine infection. It has been proved that it does not increase the rate of stillbirth.

Yaws survey on Nanumea atoll. Ira L. LeFevre, Jr., Kenneth F. McDermott and Robert B. Venner. U. S. Nav. Med. Bull., Washington, **43:** 739–741, Oct. 1944.

The authors report the investigation of yaws among natives of the Nanumea atoll in the Ellice Islands, the purpose of which was to discover the nature of primary yaws, the site and appearance of the secondary lesions, and the ages at which the Kahn test would be positive.

The 149 persons examined were divided into 3 age groups: infants under 4 years of age, children and adolescents from 5 to 16 years, inclusive, and adults over 17. Children having the lesions of yaws were given 3 weekly injections of neoarsphenamine with the standard dosage for age and

weight, after which clinical signs of the disease disappeared, though the Kahn test remained positive. Primary yaws was found only in the infant group and in the younger half of the second group. Secondary yaws was manifested by lesions of the soles of the feet and the palms of the hands. In adults, there were few evidences of active lesions. The few natives who presented tertiary yaws showed pathologic changes in the bones and joints.

The authors conclude that children nearing 3 years of age are most likely to contract yaws. Fractional injections totaling 1 gm. of neoarsphenamine according to age and weight will in most cases cause the disappearance of the clinical signs, but, as shown by the Kahn test, the disease is not eradicated. About 50 percent of the children under 16 years of age present positive evidence of the disease; the proportion increases among adolescents and is highest among adults.

Cancer of the tongue: its diagnosis and treatment. Louis H. Jorstad and D. J. Verda. Surg. Clin. North America, Philadelphia, 1077–1088, Oct. 1944.

This article, which emphasizes the importance of the early diagnosis of cancer of the tongue, states that syphilis is one of the chief lesions to be differentiated from carcinoma. A positive serologic test does not signify that the lesion of the tongue is syphilis, despite the presence of a primary, secondary, or tertiary syphilid on some other part of the body. A careful history, observation of behavior of the lesion under antisyphilitic treatment, and biopsy are essential in the diagnosis. Strict adherence to the principle that cancer of the tongue does occur in an individual with syphilis will avoid the most serious pitfall of allowing a cancer of the tongue to advance beyond the hope of eradication, while the patient is being treated for syphilis. These conditions should be treated concomitantly. The percentage of latent syphilis in patients with carcinoma of the tongue is essentially the same as the percentage of syphilis in general clinic or private practice population.

TREATMENT

Treatment of early syphilis with penicillin. A. O. F. Ross, Rachel B. Nelson, E. M. Lourie and H. O. J. Collier. Lancet, London, 2: 845–848, Dec 30, 1944.

The authors report the preliminary results obtained in 5 patients with early syphilis who were treated with penicillin and observed for 9 months. The patients selected were strongly seropositive and had well-marked secondary lesions.

The dosage schemes employed were (a) 30,000 units of penicillin given intramuscularly at 3-hour intervals for 80 injections (a total of 2,400,000 units over a 10-day period) in 4 patients, and (b) 30,000 units intramuscularly every hour for 40 injections (1,200,000 units in 40 hours) in 1 patient.

Lesions and rashes cleared up within 1 or 2 weeks. There were no toxic reactions.

Of the 4 patients receiving the maximum dosage (2,400,000 units), treatment was an unequivocal success in only 1. The patient treated with the minimum dosage of 1,200,000 units had a serologic relapse after 2 months' treatment.

Although the results of this study indicate that immediate response to treatment was favorable, the authors state that it is doubtful whether penicillin was as beneficial as arsenic-bismuth therapy might have been.

It is the opinion of the authors that penicillin treatment for syphilis will not become suitable for routine civilian practice until frequently repeated injections day and night can be avoided.

Tables are presented which give detailed results of this investigation.

Penicillin in the treatment of granuloma inguinale. Russell A. Nelson. Am. J. Syph., Gonor. & Ven. Dis., St. Louis, 28: 611–619, Sept. 1944.

The use of penicillin in the treatment of granuloma inguinale is reported in 2 patients seen at the Johns Hopkins Hos-

pital in September 1943. The one was a 33-year-old Negro laborer and the other a 43-year-old Negro. Both patients gave a history of syphilis. In each case the diagnosis of granuloma inguinale was proved by biopsy of the lesion, each showing clear-cut Donovan bodies. The first patient received 2,800,000 Florey units intramuscularly over a period of 15 days; the second patient received 1,360,000 units during 4½ days of treatment.

The patients were observed for from 30 to 40 days but showed no significant change in the lesions in either case. Donovan bodies were still present in the tissues of the first patient 27 days after therapy was begun.

Dermatitis from penicillin. George W. Binkley and Arnold Brockmore. Arch. Dermat. & Syph., Chicago, **50**: 326–327, Nov. 1944.

The authors present 2 cases of contact dermatitis, the second and third instances of this condition on record. Both occurred in the members of the medical staffs of hospitals.

The reaction in the 2 cases was not identical. In the first, the dermatitis was of a greater degree and involved a larger cutaneous area than in the second. In the second case, no epidermal or intradermal sensitivity could be shown by cutaneous tests, and the reaction obtained on deep intramuscular injection was similar to the disturbance of the fungus antigen relationship first reported by Graves, Carpenter, and Unangst. This reaction seems to occur in patients who have had a focus of dermatophytosis on the feet.

Prolonging effective penicillin action. Max Trumper and A. M. Hutter. Science, Lancaster, **100**: 432–434, Nov. 10, 1944.

A method for prolonging the therapeutic action of penicillin is described in this paper. The method depends on the delay in absorption, produced by chilling the injected muscle, with consequent prolonged vasoconstriction.

An ice bag was applied to the deltoid region 2 hours before an intramuscular injection of penicillin and for periods of 6 to 12 hours afterwards in 9 patients having gonorrhea and 1 with acute urethritis having extracellular diplococci in the discharge. Single injections of 50,000 units of penicillin in saline were administered to 7 of the first 10 patients treated; 1 patient, the tenth, received 30,000 units, and 2 received 100,000. All except the tenth maintained an adequate bacteriostatic level of the drug in the blood stream from 6 to 12 hours, and became bacteriologically and clinically negative and remained so during their period of hospitalization of 1 or 2 weeks. The tenth patient, who received 30,000 units, was a failure. Subsequently, the same technic was applied to 8 additional patients with gonorrhea, all of whom were apparently cured by a single injection of 50,000 units of penicillin.

The application of an ice bag 2 hours in advance of the injection renders the injection painless.

The method apparently effected a considerable saving in the total amount of penicillin required for the treatment of gonorrhea.

Correlation of the purity of penicillin sodium. Robert P. Herwick, Henry Welch, Lawrence K. Putnam and Armand M. Gamboa. J. A. M. A., Chicago, **127**: 74–76, Jan. 13, 1945.

At the request of the Army and the Navy, the authors undertook a study to determine the factors causing pain following intramuscular injection of penicillin. Penicillin sodium obtained from 17 manufacturing sources was administered to 230 patients, most of whom had sulfonamide resistant gonorrhea. In the first 100 patients treated, an attempt was made to correlate pain in patients following intramuscular injections with reactions following intradermal injections of the same material in man and in rabbits. In the second group of 100 patients, several manufacturers' products of varying potencies were used and injections were made into the buttocks, triceps, or deltoid. In the third group of 30 patients, each patient received

75,000 units of penicillin varying in potency from 175 units per milligram to 1,127 units. Six different concentration levels were used, and the light transmission through a red filter of the pooled samples was determined at each level, since there is some evidence that depth of color of preparation is related to purity.

The authors' conclusions are as follows:

1. A significant correlation exists between the purity (potency) of commercial penicillin sodium and irritation following intramuscular injection. With an increase in potency in units per milligram there is a corresponding decrease in the pain produced.

2. Intramuscular injection of penicillin produces a greater incidence and intensity of pain than isotonic solution of sodium chloride.

3. There is a correlation between the potency of penicillin and its light transmission. As the potency of the penicillin solutions increased, the transmission of light through the solutions also increased.

4. Of the 3 sites of injection used, the least amount of pain resulted from injections into the buttocks.

5. There is no significant correlation between the irritation produced by intradermal injection of penicillin in man or in rabbits and that produced by intramuscular injection of this material.

The intensive therapy of early syphilis. D. M. Pillsbury, C. J. Courville, R. H. Crede, J. D. Myers and C. R. Wise. Brit. J. Ven. Dis., London, **20**: 154–163, Dec. 1944.

In April 1943 intensive therapy for early syphilis was undertaken in selected United States Army hospital installations in the European Theater of Operations.

The purpose of this article is to report (1) a summary of the reasons for adopting the intensive method of treatment in military practice, (2) the technic of treatment and morbidity therefrom in a series of 775 patients personally observed by the authors, and (3) a summary of follow-up studies performed 4 months or more after completion of treatment in 435 patients.

Treatment was completed in 96.3 percent of the 775 patients. The method selected was the 20-day multiple syringe injection technic of Schoch, with many patients receiving a course of 10 bismuth injections after discharge from the hospital. Reactions causing discontinuance of treatment were, in decreasing order of frequency: secondary fever, hepatitis, toxicoderma, neutropenia, and encephalopathy. While data on serologic relapse are incomplete, the most favorable results were among the group of 205 patients with seronegative primary syphilis, there being only 1 doubtful reaction reported 4 months or more after treatment. The incidence of positive spinal fluid reactions in 236 tests performed 6 months or more after completion of treatment was less than 1 percent.

Appended to the report is the directive on penicillin therapy which was sent to all hospitals in the European Theater of Operations, United States Army, authorizing treatment with penicillin (Circular letter No. 138, Sept. 10, 1943, Office of the Chief Surgeon).

Hemorrhagic encephalitis and intensive mapharside treatment. F. L. Lydon. Brit. J. Ven. Dis., London, **20**: 87–96, Sept. 1944.

This paper gives a detailed description of the course of hemorrhagic encephalitis in each of 5 patients among 53 treated for early syphilis by an intensive course of mapharsen (mapharside) in multiple injections.

The author makes the following comments and conclusions: (1) Alcoholism may be a predisposing factor, as may also a deficiency of vitamin B_1. (2) The usual laboratory tests give no help in foreseeing the onset of encephalopathy. (3) Primary cellular damage of the brain tissue itself is a more likely pathologic development than that of the more usually accepted vascular-toxic theory. Microscopic changes in the liver found in the autopsy suggest that vitamin B_1 deficiency and the liver disorder may play important parts in the production of the damage. (4) Blood sugar curves taken during the intensive course

in 3 patients did not show any tendency towards hypoglycemia, and lumbar puncture on the fourth morning showed no change in the cerebrospinal fluid in 8 patients, although 1 of these developed encephalopathy on the eighth day. (5) Vitamin B_1 is suggested as both a prophylactic and a therapeutic agent; calcium gluconate is also used as an adjunct. Venesection, repeated lumbar puncture, and adrenalin seem to be of value. (6) Mapharsen undergoes a rapid color change in tropical climates, a change which may affect its therapeutic value, and it should, therefore, be kept under refrigeration.

Artificial fever-chemotherapy: II. arterial oxygen saturation. R. M. Craig, G. X. Schwemlein and H. Worley Kendell. Arch. Phys. Therapy, Chicago, **25**: 665–670, Nov. 1944.

This study was undertaken to determine whether a lowered arterial oxygen saturation was present in patients with early syphilis treated with fever-chemotherapy, and whether, if present, it could be corrected by the administration of oxygen. An oximeter was used for the continuous measurement of the oxygen saturation of arterial blood of 10 patients undergoing artificial fever-chemotherapy for early syphilis. The method is described.

There was invariably a lowered percentage of arterial oxygen saturation when complementary oxygen was not supplied.

The authors conclude that the use of oxygen by nasal catheter with a rate of flow of 5 to 8 liters per minute is a satisfactory and efficient method of preventing or correcting the lowered percentage of arterial oxygen saturation.

The concomitant administration of sulfathiazole and quinine or atabrine. Ben King Harned and James N. Etteldorf. Am. J. M. Sc., Philadelphia, **208**: 750–756, Dec. 1944.

The purpose of this paper is to report data on the concomitant administration of sulfathiazole and quinine or atabrine to 99 volunteer, hospitalized patients.

Of the 76 patients who completed the experimental period, 9 were not included in the tables because they represented transitional doses of drugs or deviations from the adopted routines. The data on 67 subjects are recorded and analyzed. The highest doses studied were 6 gm. of sulfathiazole daily for 7 days, 2 gm. of quinine bisulfate for the same period, and 0.3 gm. of atabrine daily for 5 days.

The following conclusions are stated:

1. The results obtained indicate that the incidence of unfavorable reactions, with the possible exception of vomiting, is not increased by the concomitant administration of sulfathiazole and quinine or atabrine.

2. The combination of drugs produced no detectable changes in the amount of hemoglobin or the total white blood cell count.

3. Quinine and atabrine produced only minor changes in the free and total sulfathiazole in the blood and in the urine.

LABORATORY RESEARCH

Studies on penicillinase. E. B. McQuarrie and A. J. Liebmann. Arch. Biochem., New York, **5**: 307–315, Dec. 1944.

This paper reports the results of studies concerning the production and activity of penicillinase, the inhibitor formed as a result of bacterial contamination of the mold fermentation used in the production of penicillin.

Three bacteria were isolated from Penicillium notatum fermentations and were labeled PD 1, 2, and 3. A method is given for the estimation of penicillinase activity and a penicillinase unit is defined. A method of extracting the enzyme from bacterial cells is described. Various media were investigated for use in growing the bacteria for penicillinase production.

The following conclusions are stated:

A 1 percent peptone medium without added sugar gave the highest yield of enzyme, but a medium containing ½ per-

ent peptone and 1 percent glucose produced the most desirable working material. Glucose could not be replaced efficiently by either sucrose or lactose in this medium.

Acetone, alcohol, dioxane, sodium tungtate, and saturated ammonium sulfate, $(NH_4)_2SO_4$, solution precipitate the enzyme. Acetone, alcohol, and dioxane inhibit the penicillinase when purified enzyme solutions are used. The enzyme is non-dialyzable through cellophane membrane.

Penicillinase in purified solution is extremely labile. It is 66 percent destroyed at 45°C. in 20 minutes and over 95 percent destroyed in an hour.

The optimum pH at 37°C. is pH 7.1.

The enzyme is inhibited by iodoacetic acid, amyl acetate, and partially by indole-3-acetic acid. It is activated by dl-phenylalanine.

Adsorption studies are given along with a purification method using adsorption and elution.

Correlation is shown between the ability of PD bacteria to produce penicillinase and their sensitivity to penicillin.

A penicillinase preparation is shown to have the same destructive action on the penicillin produced from Penicillium notatum strains NRRL-1249-B21 and NRRL-832.

The concentration of penicillin in various body fluids during penicillin therapy. Jean V. Cooke and David Goldring. J. A. M. A., Chicago, 127: 80–87, Jan. 13, 1945.

The results of observations made on penicillin levels in the blood serum and other body fluids following parenteral injections is reported in this paper. The method of testing the titer of penicillin in the body fluids has been described in another paper to be published later.

The results presented are taken from about 1,000 penicillin determinations over a period of months on about 40 patients, most of them infants and children receiving penicillin for various acute infections at 2- and 3-hour intervals in doses varying from 350 to 5,000 units per kilogram of body weight. The potency of the drug used was not routinely tested. Specimens of blood serum were taken at various intervals following injection, from 10 minutes to 3 hours, and specimens of the spinal fluid 24 hours after the intrathecal injection.

After intramuscular injections, the concentration in the blood reached its highest level within 30 minutes, remained high at 1 hour and fell rapidly during the second hour but persisted at lower titer for 3 to 4 hours.

Penicillin was found in the spinal fluid after intramuscular injection but in much lower titer than that of the blood. Apparently penicillin injected intrathecally passed readily from the spinal to the cerebral meninges but less readily from the cerebral to the spinal meninges.

The titer of penicillin in the blood and spinal fluid was found to be much higher during renal insufficiency than in the same patient when renal function was normal.

No close relationship was found between the units of penicillin per kilogram of body weight given and the concentration reached in the blood. There was some evidence that the blood concentration rose to a higher level after repeated injections than after a single dose.

Suitability of serum from recalcified human plasma for some serodiagnostic tests for syphilis. Robert D. Barnard and Charles R. Rein. J. Lab. & Clin. Med., St. Louis, 29: 1287–1293, Dec. 1944.

The authors report an investigation of the validity of the ordinary serologic tests for syphilis when conducted on recalcified human plasma, and present a satisfactory procedure for the conversion of citrated whole blood or plasma to serum based on the specific clot-inducing properties of secondary calcium phosphate.

Serologic tests on serum, citrated plasma, and recalcified citrated plasma were made. All three of these materials were found suitable for serologic testing, the latter when it was prepared either by means of calcium chloride or secondary calcium phosphate. The few instances of undoubted-

ly false biologic reactions were apparent in both citrated and recalcified plasma, though their titer was not increased by calcification, as appeared to be the case in the true syphilitic specimens.

Determinations of calcium concentration made on recalcified citrated plasma showed that clotting could be induced without an inordinate rise in calcium content.

The collection of citrated blood samples for serologic testing for syphilis was found to offer distinct advantages since citrated blood has better keeping qualities than has whole clotted blood. Comparison of whole blood and citrated blood shipped by mail showed that in citrated blood hemolysis rarely occurred, bacterial contamination was much less, and loss of reagin titer was much less than with whole blood. Serologic tests for syphilis conducted on citrated plasma or recalcified citrated plasma were found to have the same validity as those done on serum.

A comparison of the bacteriostatic activities of some of the newer sulfonamide compounds. Eleanor A. Bliss and Helen C. Deitz. Bull. Johns Hopkins Hosp., Baltimore, **75**: 1–13, July 1944.

The authors report the results of a study comparing 4 diazine derivatives of sulfanilamide with the parent compound, sulfadiazine. Besides the results of in vitro tests with sulfadiazine, sulfapyrazine, sulfamerazine, and sulfamethazine, the results of studies on dimethylacroyl sulfanilamide, dimethylbenzoyl sulfanilamide, and homosulfanilamide are included.

The bacteriostatic properties of sulfadiazine, sulfapyrazine, sulfamerazine, sulfamethazine, N_1dimethylacroyl sulfanilamide (irgamide), N_1dimethylbenzoyl sulfanilamide (irgafen) and homosulfanilamide (marfanil) were tested against one strain each of group A and group D β-hemolytic streptococci, type 1 pneumococci and E. coli, and against 5 strains of staphylococci. The authors conclude that sulfapyrazine was the most active of the diazine derivatives but its effect was percent in the twelfth grade. On reexam- involving E. coli. Homosulfanilamide belongs in a different category. It was considerably more active than the other compounds against the two kinds of hemolytic streptococci and the staphylococci and was less active against E. coli.

An intradermal reaction as an aid in the diagnosis of granuloma inguinale. Borris A. Kornblith. New York State J. Med., New York, **44**: 2476–2478, Nov. 15, 1944.

A tissue antigen was prepared from an acute lesion of granuloma inguinale which was injected intradermally into a series of 19 proved cases of granuloma inguinale and another series of control cases. In all but 2 of the 19, a positive reaction was obtained. Among the control group, 1 false positive reaction and 1 doubtful false positive reaction were obtained. A histopathologic correlation between the actual lesions of granuloma inguinale and the confirmatory skin test was demonstrated to be present. The characteristic pathology described is that of an epithelioid reaction which is common to the entire group of chronic "granulomatous diseases." The reaction to the specific intradermal test for granuloma inguinale conforms with what is to be expected in this type of disease, as does the pathologic histology.

PUBLIC HEALTH ADMINISTRATION

Army contributions to postwar venereal disease control planning. Thomas H. Sternberg and Granville W. Larimore. J. A. M. A., Chicago, **127**: 209–212, Jan. 27, 1945.

The postwar period will present far greater assets for the control of the venereal diseases than have been available at any previous time.

A tremendous number of physicians and lay personnel trained by and experienced in the Army in the principles of venereal

disease control will return to civil life and will be available as workers in connection with venereal disease control programs.

The return to civilian life of 9,000,000 soldiers who have received intensive venereal disease education will so raise the level of information on that subject among the general public that it seems certain that future programs for the control of venereal disease will receive increased support. It seems unlikely that the subject will ever again be considered unmentionable.

The remarkable advances in treatment climaxed by the introduction of penicillin therapy will add great impetus toward achieving the goal of universal case finding and case holding.

Mass wartime experiences suggest that postwar plans for the control of venereal disease will include provision for a freely available prophylaxis at a price commensurate with the cost.

These factors added to the stabilization of community life and the return of opportunity to follow the natural instincts of monogamous relationships, all lead to the conclusion that we shall be presented with an unprecedented opportunity to reduce the incidence of the venereal diseases to a manageable minimum.

Evaluation of certain educational procedures in a program for the control of venereal disease. Charles M. Carpenter, Millard E. Winchester and Allston Gourdin. New York State J. Med., New York, **45**: 281–285, Feb. 1945.

In this paper the authors attempt to evaluate the educational procedures employed during the past 3 years in a venereal disease control program in Glynn County, Georgia. Among the principal means used were health committees in Negro churches, venereal disease education in Negro schools, and posters in public lavatories. Evaluation was based on (1) questioning of patients to determine the medium that directed them to the venereal disease clinics and (2) comparison of knowledge of venereal disease among school children before and after the display of posters in the lavatories, as measured by written examination.

Interview of 604 patients who applied voluntarily for examination and treatment revealed that 461 (76 percent) reported as a result of having read one of the posters placed in public lavatories.

On a simple, 5-question examination given unannounced to children in grades 5 to 12 before the posters were placed in the lavatories, pupils' averages ranged from 15 percent in the fifth grade to 63 percent in the twelfth grade. On reexamination 6 weeks later, their answers were improved from 20 to 300 percent.

Although it could not be definitely evaluated, the work of the health committees in Negro churches also proved effective, particularly in removing the stigma attached to public mention of venereal diseases.

The authors discuss the various posters used and the principles of their construction, and compare their own experience with that of other health departments queried by letter.

Recommendations of the international conference on penicillin. Science, Washington, **101**: 42–43, Jan. 12, 1945.

An international conference on penicillin meeting in London Oct. 16-19, 1944, established an international standard for penicillin and set the international unit of penicillin in terms of that standard. The various penicillins known in Great Britain were identified as being the same as certain preparations of the drug known in the United States. The international unit was defined as the specific penicillin activity contained in 0.6 microgram of the International Penicillin Standard. This unit is approximately equivalent to the unit originally adopted by Heatley and other collaborators of Florey (1941), commonly known as the Oxford unit.

The conference recognized that it may become necessary to establish further standards made from other varieties of penicillin, and recommended that efforts should be made to make pure samples of other penicillins available for international exchange among research workers in this field.

New Cases of Syphilis and Gonorrhea in States, Territories and Possessions

Health officers' monthly statement: Reported for the first 6 months of fiscal years 1944-45 and 1943-44

Area	Cases of syphilis and gonorrhea reported for first 6 months of fiscal years below:											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44
Total United States†	†171,535	233,357	36,445	38,900	47,199	62,285	69,919	101,231	5,920	6,692	135,611	150,357
Alabama	6,757	8,739	986	1,325	1,442	2,025	1,397	2,051	151	202	3,243	3,428
Arizona	935	1,429	263	327	298	388	287	549	75	62	567	869
Arkansas	4,637	4,412	1,087	569	1,508	1,483	1,601	1,589	132	103	3,058	2,313
California	13,887	15,845	2,528	2,629	3,105	3,745	7,604	8,647	430	494	15,321	16,510
Colorado	1,337	2,178	367	508	397	623	524	958	49	89	1,136	1,678
Connecticut	1,231	1,528	121	184	592	614	238	426	38	69	566	804
Delaware	316	459	76	56	94	112	118	74	12	8	113	89
Dist. Columbia	1,700	4,070	396	498	512	1,001	653	2,383	46	65	2,155	1,886
Florida	7,665	15,556	967	1,729	2,773	4,769	3,265	7,084	211	314	6,525	8,966
Georgia	5,373	8,312	1,496	1,589	2,140	3,377	1,578	3,086	159	256	3,894	5,590
Idaho	444	294	82	140	111	56	224	75	18	4	234	441
Illinois	11,024	14,134	1,843	1,809	2,599	3,336	6,257	8,710	325	279	10,369	11,916
Indiana	2,990	4,358	610	632	400	397	1,034	1,593	107	126	1,331	1,761
Iowa	796	1,195	186	248	227	300	318	513	37	90	1,196	906
Kansas	1,303	1,316	334	253	226	272	689	741	54	50	1,342	1,008
Kentucky	2,600	3,777	636	535	604	830	961	1,619	132	154	2,345	1,788
Louisiana	5,829	9,581	1,325	1,519	1,754	2,465	1,429	2,527	239	218	5,712	6,703
Maine	425	388	84	83	53	44	174	201	34	33	883	649
Maryland	4,038	8,273	859	806	1,025	790	1,027	1,289	86	61	2,356	4,067
Massachusetts	2,097	2,820	512	589	(§)	(§)	1,474	2,073	111	158	2,174	2,581
Michigan	8,600	8,881	1,527	1,267	2,429	2,293	3,153	3,750	219	227	6,076	5,623
Minnesota	1,054	1,221	160	115	94	125	732	900	42	53	1,199	976
Mississippi	10,109	13,080	3,485	4,414	2,874	3,666	3,171	4,481	579	516	15,169	14,996
Missouri	4,588	5,101	1,010	885	1,280	1,321	1,985	2,409	155	168	4,062	2,813
Montana	219	218	45	60	21	41	58	84	5	4	155	178
Nebraska	693	670	104	105	191	354	361	161	29	22	825	832
Nevada	187	400	53	11	1	72	68	283	7	15	342	204
New Hampshire	140	113	13	15	12	31	100	57	12	4	73	100
New Jersey	4,012	5,675	600	666	1,071	1,799	2,109	2,977	180	225	2,375	2,787
New Mexico	857	991	186	216	218	223	404	499	63	53	646	744
New York	15,781	19,101	3,150	2,871	3,229	3,222	8,828	12,245	419	532	7,353	9,964
North Carolina	4,224	5,685	1,565	1,492	1,619	2,263	962	1,826	78	104	4,574	4,589
North Dakota	101	159	22	53	15	26	36	51	7	9	177	149
Ohio	9,634	11,758	2,042	1,773	2,635	2,790	4,538	5,933	419	481	3,327	2,686
Oklahoma	3,636	3,953	563	508	927	1,148	1,167	1,424	127	148	3,768	2,435
Oregon	998	1,020	267	299	111	83	573	606	38	32	1,234	1,218
Pennsylvania	5,566	6,740	1,007	882	1,802	2,638	1,823	2,457	223	330	0	614
Rhode Island	443	556	100	42	42	58	214	402	21	12	735	379
South Carolina	4,071	7,974	1,140	1,657	1,344	3,269	1,271	2,665	158	195	3,347	3,403
South Dakota	208	254	29	51	60	35	91	121	23	24	250	208
Tennessee	6,979	9,159	1,139	1,234	2,671	3,731	2,760	3,897	225	201	5,913	7,687
Texas	6,851	11,044	1,467	1,454	2,392	3,237	2,346	4,281	253	284	4,508	5,230
Utah	291	467	88	120	23	65	174	274	6	8	272	331
Vermont	85	134	10	44	25	40	36	45	9	5	204	90
Virginia	4,561	7,320	1,377	2,171	1,840	2,772	1,183	2,112	106	138	2,646	6,346
Washington	(*)	2,294	(*)	444	(*)	531	(*)	1,011	(*)	63	(*)	4,481
West Virginia	945	1,848	320	318	129	266	201	390	25	48	1,205	1,155
Wisconsin	444	485	101	92	0	0	332	389	11	4	553	580
Wyoming	874	686	117	57	284	90	391	324	35	15	103	87
Territories, Possessions and Canal Zone												
Alaska	48	43	18	28	9	7	11	4	1	1	256	228
Canal Zone	448	(*)	61	(*)	88	(*)	249	(*)	15	(*)	267	(*)
Hawaii	341	406	96	71	43	58	176	294	18	22	697	816
Puerto Rico	5,381	8,579	798	842	1,824	1,772	1,512	2,817	1,157	1,057	2,863	2,014
Virgin Islands	129	117	28	24	74	69	20	18	2	6	46	196
Actual total# U. S. and Possessions	177,882	244,796	37,446	40,309	49,237	64,722	71,887	105,375	7,113	7,841	139,740	158,092

*No data available.
**Includes "not stated."
†Based on States reporting in both fiscal periods.
#Includes all reported cases.
§Included in late latent.
‡Based on 47 States and District of Columbia.

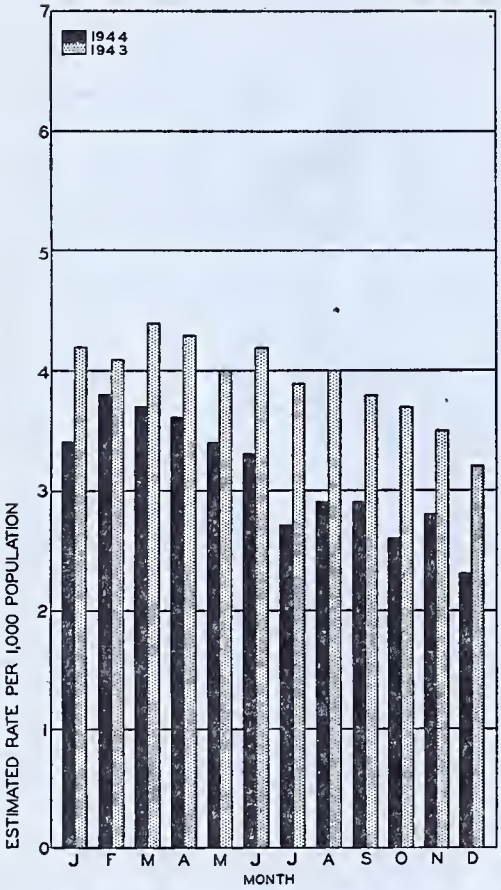
New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over

Health officers' monthly statement: Reported for the first 6 months of fiscal years 1944-45 and 1943-44

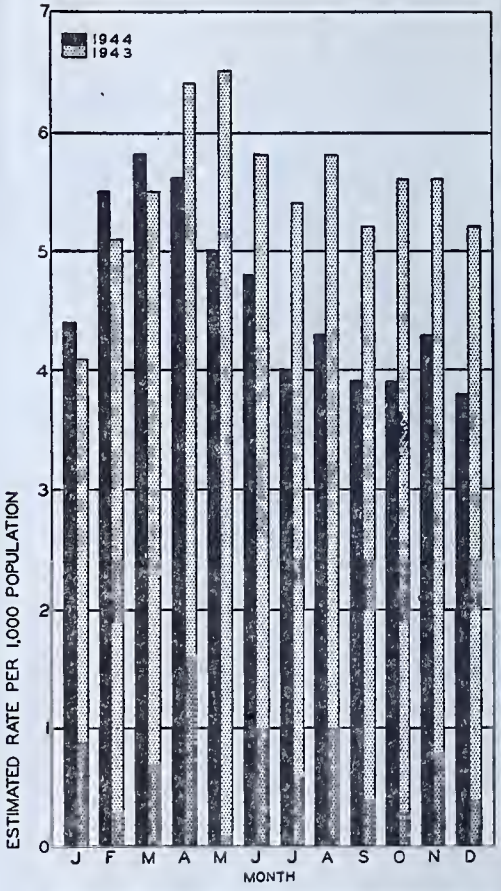
City	Cases of syphilis and gonorrhea reported for first 6 months of fiscal years below:											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44
Total†	[1]63,715	[1]85,990	[2]12,688	[2]9,836	[2]14,907	[2]18,239	[2]28,951	[2]37,960	[2]1,575	[2]1,565	[1]45,326	[1]39,728
Akron	496	461	123	65	108	117	234	256	31	23	328	177
Atlanta	1,320	1,557	361	367	383	461	552	712	24	19	1,517	654
Baltimore	2,753	6,683	717	611	731	560	870	984	38	34	1,488	1,524
Birmingham	1,541	2,729	214	172	382	713	398	583	38	48	393	329
Boston	754	895	178	178	80	0	390	574	29	22	784	664
Buffalo	879	1,021	138	122	124	129	588	744	29	26	538	439
Chicago	7,565	7,602	1,351	1,219	1,886	1,841	4,137	4,388	191	154	7,106	6,620
Cincinnati	1,207	1,644	201	210	(§)	(§)	1,006	1,434	0	0	556	507
Cleveland	2,094	2,064	438	385	657	653	952	977	47	49	926	729
Columbus	718	764	217	153	162	161	311	410	28	20	232	159
Dallas	961	1,261	243	233	269	272	443	746	6	10	413	394
Dayton	536	990	63	114	195	275	260	570	18	31	275	364
Denver	626	1,014	179	212	200	263	211	390	19	30	570	929
Detroit	4,998	6,093	993	762	1,739	1,881	2,165	3,345	101	105	2,925	2,934
Honolulu	125	236	30	39	15	36	69	144	6	17	484	577
Houston	(*)	955	(*)	157	(*)	330	(*)	436	(*)	32	(*)	1,150
Indianapolis	886	1,084	173	301	115	10	220	254	13	14	205	44
Jersey City	198	285	24	26	59	56	102	196	13	17	39	25
Kansas City	685	913	138	152	159	158	337	566	32	35	530	474
Los Angeles	5,369	5,747	1,465	0	399	2,265	3,342	3,313	163	169	3,433	2,531
Louisville	635	1,114	194	157	134	201	263	472	19	13	736	443
Memphis	2,990	3,309	390	289	1,415	1,563	1,070	1,414	115	43	2,518	2,876
Milwaukee	284	245	46	29	(§)	(§)	234	202	5	1	210	99
Minneapolis	303	324	76	52	47	57	170	207	10	6	529	400
Newark	877	1,146	172	132	288	295	402	685	25	34	636	460
New Orleans	712	1,605	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	979	1,181
New York	11,307	13,206	2,557	2,328	2,768	2,917	5,613	7,476	274	336	7,353	7,135
Oakland	(*)	790	(*)	93	(*)	190	(*)	479	(*)	20	(*)	691
Oklahoma City	(*)	1,108	(*)	104	(*)	308	(*)	338	(*)	19	(*)	475
Omaha	275	298	52	22	57	183	158	68	8	18	242	257
Philadelphia	3,019	5,458	401	164	578	614	807	762	84	52	514	451
Pittsburgh	756	4,281	135	(*)	202	(*)	375	(*)	44	(*)	163	46
Portland	447	449	159	111	49	29	232	304	7	5	861	490
Providence	226	274	22	49	27	21	125	181	10	4	90	87
Rochester	149	134	34	26	8	12	105	93	2	3	214	147
St. Louis	2,940	2,996	595	401	931	1,038	1,326	1,454	88	93	2,081	921
St. Paul	118	154	18	20	21	27	64	97	6	3	146	158
San Antonio	(*)	590	(*)	63	(*)	163	(*)	344	(*)	18	(*)	684
San Diego	654	652	98	55	193	184	279	368	28	24	596	452
San Francisco	1,272	1,519	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,303	1,084
Seattle	738	700	164	85	176	130	382	439	9	11	954	851
Syracuse	325	521	30	15	12	20	279	471	4	15	218	158
Toledo	277	492	38	82	28	96	202	298	9	16	86	72
Washington, D. C.	1,700	4,070	396	498	512	1,001	653	2,383	46	65	2,155	1,886
Actual total#	63,715	89,433	12,823	10,253	15,109	19,230	29,326	39,557	1,619	1,654	45,326	42,728

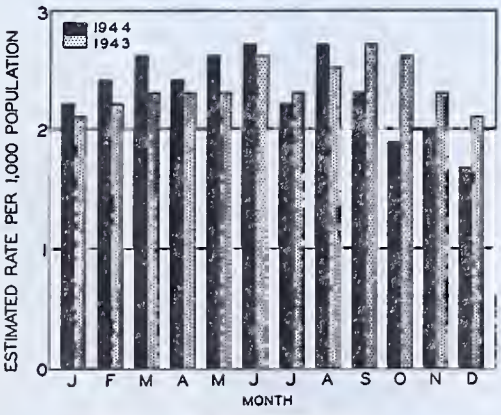
*Data not available.
**Includes "not stated."
†Based on cities reporting in both fiscal periods.
#Includes all reported cases.
§Included in late latent.
[1]Based on 40 cities.
[2]Based on 37 cities.

ANNUAL SYPHILIS CASE RATES
IN THE UNITED STATES
BASED ON PROVISIONAL MONTHLY DATA
1944 AND 1943

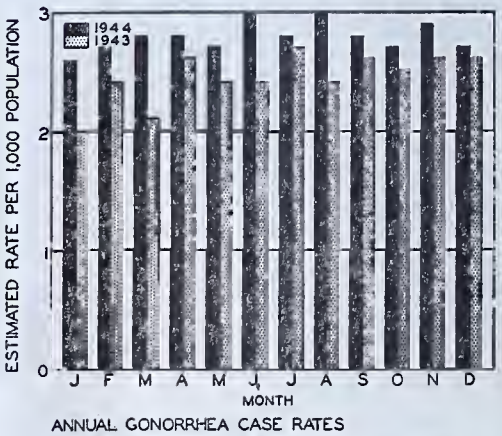


ANNUAL SYPHILIS CASE RATES
IN CITIES OF 200,000 POPULATION AND OVER
BASED ON PROVISIONAL MONTHLY DATA
1944 AND 1943





ANNUAL GONORRHEA CASE RATES
IN THE UNITED STATES
BASED ON PROVISIONAL MONTHLY DATA
1944 AND 1943



ANNUAL GONORRHEA CASE RATES
IN CITIES OF 200,000 POPULATION AND OVER
BASED ON PROVISIONAL MONTHLY DATA
1944 AND 1943

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Venereal Disease Information

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FEDERAL SECURITY AGENCY

UNITED STATES PUBLIC HEALTH SERVICE

THOMAS PARRAN, *Surgeon General*

Editor: J. R. HELLER, Jr., *Medical Director*
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Penicillin in Gonorrhea

The present issue of Venereal Disease Information is devoted to three icles dealing with current experience in the treatment of gonorrhea. The st. by Thomas and Meyer, presents two schedules of treatment involving usual aqueous solution of penicillin sodium and two schedules involving gle injections of penicillin in a mixture of beeswax and peanut oil. The ond, by Van Slyke and Heller, presents the results of a cooperative study the use of a single injection of penicillin in beeswax and peanut oil. The rd, by Graham, Greenblatt and Cannefax, discusses the use of a single ection of penicillin in a refined wax-oil mixture similar to the beeswax and anut oil used by other workers.

All of these schedules were developed to fit the needs of the private physician d outpatient clinic where treatment must be completed in a relatively short ace of time. Many of the cases included in the cooperative study reported the second article were actually treated in offices and outpatient clinics, d the four-hour "schedule B" described by Thomas is well adapted to such nditions. The latter is, at the present time, the most practical for general use, ace it is carried out with sodium penicillin in aqueous solution which is adily available throughout the country. The various oil-wax mixtures have t as yet been standardized, are not commercially available, and are not easily epared.

One word of caution is in order. Although there has not as yet been monstrated any tendency for Neisseria gonorrhoeæ to develop penicillin stness in vitro, nevertheless this phenomenon may eventually occur and may cessitate reevaluation of the antibiotic. Some workers have had less success th the penicillin treatment of gonorrhea than was observed in the present ports. Also, there has as yet been no conclusive report concerning the pos- le development of asymptomatic carrier states following penicillin therapy. evertheless, at the present time and pending further investigation of such oblems, aqueous solutions of penicillin given in three or more intramuscular jections over a period of approximately four hours, or oil-beeswax suspen- ns of penicillin given in single injections, seem to provide suitable therapy r gonorrhea. At least, the present unsatisfactory response to the sulfonamides stifies a change to penicillin even though it may not be the final solution the problem of treating this disease.

—The Editors.

Penicillin in the Treatment of Gonorrhea

Results With Six Hundred and Seventy-five Women

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and

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This report on the results of treatment of gonorrhea relates our experience with 797 women, all hospitalized at the Rapid Treatment Center, Bellevue Hospital, New York City, during the period from May 1, 1944, to Mar. 1, 1945. Six hundred and seventy-five of the women received penicillin, and 122 received sulfonamides. The total group is subdivided for study into smaller units according to type and schedule of therapy, but in all other respects it has remained uniform throughout the period of observation. That is to say, criteria of diagnosis and cure were identical, and the patients were drawn by the same methods from the same type of social and racial background. Most of the women were brought in under one or another form of detention. This situation arises from the case-finding methods in use. In many instances the gonococcic infection is first discovered by routine examination when these women are brought to the attention of law-enforcement or social protective agencies as the result of suspicious conduct. Those whose infectiousness is established are held under quarantine until they have passed the tests of cure. No patient is included in this series who did not eventually pass such tests. The racial composition of the group is approximately 3 Negro to 2 white women, the latter including a fair proportion of Puerto Ricans. Sexual promiscuity is practiced by the majority of these individuals; therefore, few are able to give reliable histories, even when they have full information about their contacts.

Since epidemiologic evidence is only occasionally trustworthy, and clinical evidence is presumptive, definite diagnosis, both of the original infection and of treatment failure, rests on the recovery of the gonococcus by cultures. These are made by direct inoculation of the urethral and cervical sec tions on plates of Difco proteose pept No. 3 agar enriched with 12 percent ho blood laked with distilled water. Pla are incubated in candle jars at 35° C. 45 hours. Identification rests on type growth, a positive oxidase test, and char teristic morphology in the gram-stai smear. In cultures where growth is aty cal, or in other instances where the id tity of the organism is still in doubt, s cultures are made and tested by growth nutrient agar and by sugar fermentati reactions. This procedure is also the r in all positive cultures which repres treatment failures, since it has been fou in 3 instances that the infection, apparen gonococcic and resistant to 2 courses therapy, was actually due to N. pharyn sicca. Four posttreatment cultures a taken on alternate days, beginning the d following termination of treatment wi penicillin and 3 days after termination treatment with sulfathiazole. The occu rence of a positive culture at any time aft treatment was considered to indicate treatment failure.

A large proportion of the women in t series probably had chronic gonorrh There were few instances where the ons of infection could be determined accurate because most patients had no sympto either present or past. Though many h the clinical sign of vaginal discharge varying amounts, few could give a cle history of its onset or of any sudden i crease, or could recall urinary disturbanc Some few had symptoms pointing to i volvement of the pelvic organs, but the incidence did not correspond to the great number in whom more or less marked cli ical signs could be found. Some degree chronic cervical infection was the rule.

st chronic cases the period of hospital-tion was too short to permit perceptible nge in the clinical signs of infections. wever, in patients with acute infections in those with noticeable complications, response was usually evident and some-es dramatic.

After the use of penicillin became rou-e, the drug was given to all women as n as the diagnosis was made, without eliminary recourse to sulfonamide ther-y. Complicated or sulfonamide resistant ections were rendered culture-negative penicillin as readily as uncomplicated es, and by the same dosage. Clinical im-ovement in the former was slow, though the majority it began promptly after atment. In a few cases, particularly se with severe pelvic inflammatory dis-e or arthritis, treatment was repeated th larger doses, because, although the cteriologic response was satisfactory, the nical improvement was not. In this ies no additional benefit was observed m the administration of more than 300,-0 units of penicillin.

Very few reactions to penicillin have de-loped in this group. Those which did cur were urticarial, and all but 2 ap-ared soon after the completion of treat-ent. One girl, who failed to respond to nicillin in oil and beeswax and was re-eated with the aqueous solution, devel-ed a large nontender area of redness and elling at the site of the oil injection, 5 ys after the end of the second treatment. is subsided within 3 days. The second rl received 2 courses of treatment with ueous solution, 6 months intervening be-een the first and second course; 8 days llowing the second course she developed neral superficial edema, lasting about a eek, with mild laryngospasm at the onset. 2 patients, a mild rise of temperature ter penicillin treatment for gonorrhea dicated a concomitant early syphilis.

From May 1 to June 20, 1944, 122 girls ere treated with sulfathiazole by the usual utine. Failures were retreated with pen-illin and subsequently passed tests of cure. he results are tabulated.

After June 20, penicillin replaced sulfa-iazole as routine therapy. Sodium peni-

TABLE 1.—*Results in women treated with 1 course of sulfathiazole*

	Patients treated	SUCCESS		FAILURE	
		Number	Percent	Number	Percent
White..	45	30	67.0	15	33.0
Negro..	77	67	87.0	10	13.0
Total.	122	97	80.0	25	20.0

cillin, employed in all schedules except C and D described below, was obtained through Bellevue Hospital from a number of different commercial manufacturers and was used soon after its arrival in the hospital. Two different time-dose schedules were followed.

Schedule A, used from June to Nov. 15, 1944, consisted of 5 intramuscular injections of 20,000 units of sodium penicillin each in aqueous solution given at 3-hour intervals. Two hundred and seventy-five women were treated in this way. Those from whom the gonococcus could still be recovered by culture were retreated with 8 injections of 25,000 units each, at 3-hour intervals. Up to the present time, no gonococci have been obtained from any patient after the latter treatment.

Schedule B, used from Nov. 15, 1944, to Mar. 1, 1945, consisted of 3 intramuscular injections of sodium penicillin in aqueous solution of 50,000 units each, 2 hours apart. The results for 185 women are shown in table 3.

The patients who failed to respond to schedule B were all rendered culture-negative by 1 retreatment with penicillin.

TABLE 2.—*Results in women treated with 100,000 units of sodium penicillin in 5 doses of 20,000 units 3 hours apart*

SCHEDULE A

	Patients treated	SUCCESS		FAILURE	
		Number	Percent	Number	Percent
White..	133	128	96.2	5	3.8
Negro..	142	136	95.8	6	4.2
Total.	275	264	96.0	11	4.0

Three of them received a total of 150,000 units in 7 injections, and 2 received 200,000 units in 8 injections, all injections at 3-hour intervals.

TABLE 3.—*Results in women treated with 150,000 units of sodium penicillin in 3 injections of 50,000 units 2 hours apart*

SCHEDULE B

	Patients treated	SUCCESS		FAILURE	
		Number	Percent	Number	Percent
White..	76	71	93.0	5	7.0
Negro..	109	109	100.0	0	0.0
Total.	185	180	97.3	5	2.7

TABLE 4.—*Results in women treated with 150,000 units of calcium penicillin in oil and beeswax in a single injection*

SCHEDULE C

	Patients treated	SUCCESS		FAILURE	
		Number	Percent	Number	Percent
White..	13	13	100.0	0	0.0
Negro..	36	34	94.4	2	5.6
Total.	49	47	96.0	2	4.0

TABLE 5.—*Results in women treated with 200,000 units of calcium penicillin in oil and beeswax in a single injection*

SCHEDULE D

	Patients treated	SUCCESS		FAILURE	
		Number	Percent	Number	Percent
White..	81	67	82.7	14	17.3
Negro..	85	73	85.9	12	14.1
Total.	166	140	84.3	26	15.7

With schedule C, the use of calcium penicillin in peanut oil containing 4 percent beeswax was started. A suspension containing 100,000 units per cubic centimeter, prepared according to the method of Romansky and Rittman (*1*), was furnished by a pharmaceutical laboratory. The do was 1½ cc. in a single intramuscular i jection, or 150,000 units, as nearly as cou be measured. We encountered some difi culties in handling this preparation at firs but these were soon overcome. A seri of 50 girls were treated in this way, 1 whom did not undergo tests of cure. R sults with the remaining 49 appear table 4.

With schedule D the dose of calciu penicillin in peanut oil with 4 percent bee wax was raised to 200,000 units in a sing injection. The suspension was of the sam composition and was obtained from th same source as that used in the precedin schedules. One hundred and sixty-si women were treated and were held for minimum of 5 cultures as test of cure. B cause there appeared at first to be som difference in the effectiveness of differe lots of the suspension, 6 failures resultin from treatment with an early lot were r treated with another. Three of these the met tests of cure. Of 166 patients treate 26 failed on 1 course; of 175 treatmen given, 29 failed. All failures eventuall passed tests of cure after 1 treatment wit 200,000 units of commercial sodium penici lin in aqueous solution given in 8 injectio 3 hours apart.

Since the results obtained by the use schedule D were less favorable than thos by schedule C, the question arises whethe the fault may have been with the lot of pe icillin used in schedule D.

In the entire series of 675 women treate with penicillin, 44 failed of cure after the initial course. Three of these failed to r spond to a second course, making a total 47 treatment failures observed.

As it is of great practical importance t know what proportion of failures would b overlooked if the number of posttreatme cultures were reduced, the results of th posttreatment cultures taken on each of th uncured cases are tabulated below. Tw additional failures observed with a diffe ent schedule are included, making a tot of 49.

Of 29 failures in the series in which or more cultures were required, 3 (10 pe cent) were detected by performing mo

n 3 tests of cure. If this procedure had n routine in the entire series of 675, er factors remaining constant, 2 more ures might have been found. The first ttreatment culture detected 65 percent failures, the second, an additional 16 cent.

DISCUSSION

Our experience demonstrates that on the ne time-dose schedules, as large a proportion of gonococcic infections of all types can be rendered culture-negative in women with penicillin therapy, as in men (*2*). It has already been shown that this is true of sulfonamide therapy, but that in both sexes results differ according to race (*3, 4*). That is, among patients treated during 1942 and 1943, largely in the southern States, about 30 percent more Negro patients were "cured" than white. The small series of sulfonamide–treated women in this report is included for comparison, as it deals with patients found in a large city, where, because of the prevalence of selftreatment, a high proportion of resistant strains of gonococci might be encountered. The series shows results in Negro girls definitely superior to those in white, though the span between the two (20 percent) is not so wide as elsewhere. Having had our attention focused on the racial difference in response to treatment, we watched for the same phenomenon in the patients treated with penicillin. It did not occur. Although the total number of failures is hardly large enough to furnish statistical evidence, the proportions by race are roughly equivalent to the proportions treated. This agrees with the observations of Sternberg and Turner in the treatment of men (*2*).

The failure to identify the infecting organism by sugar fermentation reactions in all cases before treatment introduces a possible source of error in the whole series. Since the little evidence at present available suggests that the gonococcus and meningococcus are more susceptible to penicillin than other members of the genus Neisseriae, the bias would be in the direction of a high failure rate. This is more than offset, however, by the practice of making confirmatory tests on all cultures representing treatment failures. Hence, the end result is a bias of unknown but probably small dimensions in favor of high cure rates.

In promoting the rapid treatment of gonorrhea, schedules which can be carried out in one visit or in a few visits falling within the period of one clinic session have great practical advantage. The schedule of 3 doses at intervals of 2 hours meets these requirements and has proved efficient enough to warrant its further trial, pend-

BLE 6.—*Results of posttreatment cultures, in 49 treatment failures*

Failure	Culture number					
	1	2	3	4	5	6
	Culture report					
	+	+	+	+		
	+	+				
	−	−	−	+	−	−
	+	+	+			
	−	−	+	−		
	+	−	−	+		
	−	+	+	+		
	+	+	+	+		
	+	+	+			
	+	+	+	+		
	+	+	+	+		
	+	+	−	−		
	+	+	−	+	−	
	+	+	+			
	+	+				
	−	+	+			
	+	+	+			
	−	+	+			
	+	−	−	−	−	+
	−	+	+			
	−	−	+	+	+	
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	−	+	−	−		
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	+	−				
	−	+				
	+					
	−	−	+	−		
	+	−				
	+	+				
	−	−	−	+		
	+	+	+			
	+	+	+			
	+	+	+	−		
Number of cases first positive on each culture	32	8	5	4	0	0

ing final appraisal of the single injection methods depending on means of prolonging absorption of the antibiotic.

SUMMARY

1. Commercially produced sodium penicillin, administered according to identical time-dose schedules, is as efficient in the treatment of gonorrhea in women as in men.

2. No difference in response to treatment can be demonstrated in different races.

3. No naturally penicillin fast strain of gonococcus has been encountered nor any indication of the development of penicillin fastness under treatment.

4. With sodium penicillin, which is no available, a 4-hour treatment schedule suit able for use by private physicians and clin ics has proven satisfactory.

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Treatment of Gonorrhea by a Single Intramuscular Injection of Penicillin-oil-beeswax

A Cooperative Study of 1,060 Cases

C. J. Van Slyke, M.D.,[1] and J. R. Heller, Jr., M.D.[2]

Following the report of Romansky and Rittman[3] that a single intramuscular injection of penicillin calcium suspended in an oil-beeswax mixture was effective in the treatment of gonococcic infections, arrangements were made to explore further this means of therapy in order to determine not only its effectiveness but also the applicability of such a method in a widescale attack on gonococcic infections. It is the purpos of this paper to report the results and con clusions of the study. The investigatio was entirely a cooperative endeavor. A diagnoses, treatments, and posttreatmen observations were the responsibility of th cooperating physicians whose assistance gratefully acknowledged and who are name following the body of the paper. Th authors accept the responsibility of organ izing and administering the study and fo the preparation of this report.

In order to secure uniform criteria o diagnosis and reports on response to ther apy, a letter describing the study as com pletely as possible was sent to each physi cian invited to participate. The followin are the essential portions of this letter:

[1]Senior Surgeon, Assistant Chief, Venereal Disease Division, U. S. Public Health Service, Washington, D. C.

[2]Medical Director, Chief, Venereal Disease Division, U. S. Public Health Service, Washington, D. C.

[3]Romansky, M. J.; Rittman, G. E.: Penicillin. 1. Prolonged action in beeswax-peanut oil mixture. 2. Single injection treatment of gonorrhea. Bull. U. S. Army M. Dept., No. 81: 43-49, 1944.

"January 4, 1945

ear Doctor:

The published report (1) of Romansky . Rittman, M.C., U. S. Army, has indi-ed the value of a single intramuscular ection of a suspension of calcium peni-in-peanut oil-4% beeswax in curing ococcic infections in men. . . . Toxicity s notably absent. There appeared to be n less pain immediately after injection n with saline or water solutions of peni-in, although there was slight local sore-s 24 hours later only.

If these preliminary results are con-ned it appears that the treatment of the k of gonococcic infections can be con-ted expeditiously in the offices of physi-ns in private practice or in clinics. It is refore the aim of the U. S. Public alth Service to evaluate on a broad basis s newer method of therapy for gonococ-infections as rapidly and carefully as sible. Your cooperation in this study is ited and will be appreciated. If you l it possible to assist in this study the icillin suspension will be supplied by the S. Public Health Service. This sus-nsion is a sterile mixture of calcium peni-lin in peanut oil and 4 percent white eswax so prepared that 1 cc. contains),000 Oxford units of penicillin. The cal-m salt of penicillin is employed instead the sodium salt since it is less hygro-pic and more readily uniformly dis-rsed in this oily mixture. There is no parent difference in toxicity between the lcium and sodium salts of penicillin. Ex-nsive animal experimentation has shown at the beeswax disappears from the site injection within a few days and has not own any tendency to provoke any foreign dy reaction, and as you are undoubtedly are peanut oil has long been used for the spension of bismuth subsalicylate for in-muscular injection.

. It is proposed to give 200,000 Oxford its (2 cc.) intramuscularly as single in-ction into the upper and outer quadrant a buttock. . . .

. . . . At room temperatures the mixture ay not be sufficiently fluid for injection, d it may be necessary to warm the sus-nsion. This is satisfactorily accomplished ther by placing the capped penicillin bot-e in the incubator at 37° C. or by partial mmersion in a pan of water which is hot the hand (approximately 40° C.) for a me sufficient to establish ample fluidity of e mixture when a portion of the contents ay then be aspirated, under sterile pre-utions, through the rubber cap by means an 18 gauge, 2–2½ inch needle. Because the penicillin suspension is usually dark in color and may prevent detection if blood is aspirated, it is advised that a separate dry syringe fitted with a 19 or 20 gauge, 2–2½ inch needle be inserted intramuscularly and negative tension be applied in order that intravenous administration of the oily mixture be avoided. The syringe containing the penicillin can now be substituted for the dry syringe and the injection accomplished. Massage of the injection site is to be avoided in order not to interfere with the delay in penicillin absorption.

"5. . . .

"6. The selection of patients is not to be limited either to sex or to race. It is, however, extremely important that you select for this treatment only those patients whom you deem suitable from the point of view of control during the posttreatment observation period in order that subsequent exposures may not confuse the therapeutic results. Further, in the selection of patients it is not necessary that the patient first be treated with any of the sulfonamide compounds or that the infections be uncomplicated.

"7. For the purposes of the investigation it is essential that the diagnosis be confirmed by culture studies. (Differential carbohydrate tests are not required for diagnosis). This does not mean, however, that you are asked to delay treatment pending the receipt of the results of culture studies. With the proper selection of patients it can reasonably be expected that necessary elimination of cases treated with cultures subsequently reported as 'negative' will be at a practical minimum. In chronic infections, particularly in women, it is suggested that treatment be withheld pending cultural confirmation of the diagnoses. In this connection it must be noted the demands of an intensive investigational study of this type may appear distinctly contrariwise to your conception of the demands of general control of this disease.

"8. . . .

"9. The 'tests of cure' are to be left entirely to your professional judgment, but for purposes of establishing minimum standards it has been decided that a case cannot be included in this evaluation unless there has been a posttreatment observation period of at least ten days and that there be at least three negative culture reports following therapy—this includes the final culture secured on the last day of posttreatment observation. . . .

"10. For those patients failing to be cured it is requested that the record in this case be forwarded promptly to this office. In women particularly it is necessary that so-called positive cultures be checked by differential carbohydrate fermentation tests

"(1) Bulletin of U. S. Army Medical Department, October, 1944.

before a final judgment of failure of therapy is made. This is required since certain nonpathogenic diplococci are sometimes found in the genital tract and may be termed 'gonococci' unless their true identity be determined.
"11. . . .
"12. . . .
"13. Merely as a reminder your attention is called to the possibility of this penicillin therapy being sufficient to depress or alter the usual evidence of a syphilitic infection acquired concomitantly with the gonococcus infection. Penicillin therapy for gonorrhea, which is subminimal for syphilis, has been reported as lengthening the incubation period of syphilis, in some instances for more than 60 days.
"14. . . .
"15. . . .
"16. . . ."

As indicated above, this letter established fairly adequate standards and procedures for the selection of patients, the diagnosis of the infection, the minimal demands of the criteria of cure, the technic of administering treatment and for reporting the results as well as any reactions to the treatment. (The chart shows the report form employed.)

It will be noted that sugar fermentation tests were required as confirmation of posttreatment cultures but not of diagnostic cultures. This may introduce some small bias toward a reduction of the failure rates. However, it is probable that not more than about 4 percent of cases failing to respond to penicillin treatment were caused by nongonococcic organisms thus identified.

The participating physicians represented all sections of the country. They reported on the treatment of 1,060 persons, approximately 63 percent of whom were of the white race; males comprised 38 percent of the total number of patients.

The records indicate that the relief of subjective symptoms and disappearance of discharges, swellings, etc., was satisfactory and did not differ in any way from the results usually obtained by the use of adequate amounts of sodium penicillin in aqueous or saline solution. There were reported three cases of arthritis of slight degree. Two of these patients appeared to be relieved immediately by the intramuscular therapy while the third required further treatment for the arthritis, although the infection of the genital tract appear to have been eradicated.

There were only very few comme recorded as to local soreness follow therapy. There were no reports of p sistent nodules or infection at the site the injection. There were three instances sensitization reactions. One of these v very mild, one was a generalized erupti and one a more localized eruption involv the hands and feet and persisting for ab 6 days. According to the records th were no other toxic reactions.

The table records the results of tre ment of all cases. Analysis indicates t sex, race, or resistance to previous thera was without significant effect on the tre ment response. For various reasons it w not possible in all instances to satisfy t diagnostic demands of the study. The tab therefore, separates the patients into groups: Group A, those with a satisfacto culture diagnosis, and group B, those whom the diagnosis was not confirmed culture studies. Further definition of t terms used in the table follows:

"Cured" means that the case satisfied t criteria of cure set forth in the lett sent to the participating physicians at t start of the study.

"Probable cure" means that the posttrea ment observation period was less than days, or that there were only 2 negati cultures, or both, but that the patient w considered by the treating physician to cured on the basis of clinical judgme despite the limited bacteriologic and po treatment observation.

"Failure" means that following treatme cultures positive for Neisseria gonorrhoe and confirmed by differential carbohydra fermentation tests were obtained.

"Probable failure" means that the patie was considered as failing to respond treatment on the basis of a positive cultu not confirmed by carbohydrate fermentati tests, a positive smear, or the clinical jud ment of the attending physician.

"No case" refers to a patient lapsi posttreatment observation too soon to pe mit a valid opinion as to probable resul of therapy.

"Previously treated" means that t

FEDERAL SECURITY AGENCY
S. PUBLIC HEALTH SERVICE
VM-1258

BUDGET BUREAU NO. 68-450:
Approval expires 5-15-45

COOPERATIVE INVESTIGATION

SINGLE INTRAMUSCULAR INJECTION OF 200,000 OXFORD UNITS OF CALCIUM PENICILLIN IN PEANUT OIL - 4% BEESWAX

PATIENT IDENTIFICATION: _____ Your Case No. _____
(Name or other identification) (Begin with #1)

DIAGNOSIS (include complications, indicate severity) _____

_____ Made on (date) _____

By: History ☐ Clinical symptoms ☐ Positive smear ☐ and/or Positive culture ☐

DURATION OF GC: _____ days or Unknown ☐ SEX _____ RACE _____ AGE _____

PREVIOUS TREATMENT FOR THIS INFECTION: _____

_____

PENICILLIN GIVEN - Date: _____

POSTTREATMENT OBSERVATION

1945		Laboratory Results		Clinical Response*
Month	Day	Smear	Culture	

(*Report toxicity, local reaction, disappearance of discharge, response of complications, etc.)

RESULTS OF THERAPY: _____ Date: _____

Failure established by: Clinical symptoms ☐ Pos. smear ☐ Pos. culture ☐ Ferment. tests ☐

PHYSICIAN _____

ADDRESS _____

PLEASE transmit this record promptly on termination of 30 days of posttreatment observation to U. S. PUBLIC HEALTH SERVICE, WASHINGTON 14, D. C.

TABLE

	Group A Satisfactory culture diagnosis					Group B No culture diagnosis				
	Cured	Probable cure	Probable failure	Failure	No case	Cured	Probable cure	Probable failure	Failure	No case
Male—white, untreated	68	21	3	4	3	27	3	1	1	4
Male—white, previously treated	56	10	2	4	1	24	5	—	1	3
Female—white, untreated	172	9	5	21	2	12	8	1	—	1
Female—white, previously treated	138	8	2	4	1	3	2	1	—	—
Male—Negro, untreated	39	8	—	1	1	20	2	5	—	1
Male—Negro, previously treated	22	10	—	1	—	6	4	—	—	2
Female—Negro, untreated	197	11	3	22	—	2	9	1	1	3
Female—Negro, previously treated	20	1	1	3	—	2	—	—	—	—

patient had received therapy other than penicillin for the same infection prior to the administration of the treatment included in the present study.

In addition to the 1,029 patients listed in the table there were 31 patients who did not have culture studies at any time in the diagnostic or posttreatment period. A rigorous application of preestablished criteria of diagnosis and of cure excludes these patients from consideration, although the diagnosis appears to be justified on the bases of clinical evidence and the results of the examination of stained smears. All of these 31 patients appeared to respond favorably.

From the table it can be determined that if consideration is given only to the patients in group A who are classified definitely as "cured" or "failures" the cure rate is 92.2 percent. If, however, the "probable cures" and "probable failures" are included the cure rate becomes 91.2 percent. The inclusion of similar cases from group B leaves the cure rate at 91.2 percent.

The cure rates quoted above are based on the therapeutic results of a single intramuscular injection. In many of the failure cases a second injection of penicillin-oil-beeswax produced favorable results, or the patient was cured by multiple injections of sodium penicillin in water or saline solution.

Although it is clear that the cure rates stated are based on a minimal acceptable number of culture studies and posttreatment observation, it may be mentioned that 53 of the cured patients were observed for a period in excess of 1 month and received an average of more than 6 culture studies each.

Of greater influence than the period of observation, however, on the so-called "cure rate" is the lack of patient control or reliable information concerning his or her actions during the posttreatment observation period. Although it is recognized that possibly some instances of reinfection during the posttreatment period are considered as failure to respond to the therapy under investigation, it is not deemed advisable to evaluate these patients as other than failure cases. In the group of patients under report there were numerous instances in which the participating physician presented evidence of reexposure during the posttreatment observation period, even to the original source of the infection. This fact may be considered to counterbalance the bias, already mentioned, toward lowered failure rates brought about by the lack of sugar fermentation tests in confirmation of all diagnostic cultures.

SUMMARY AND CONCLUSIONS

1. The results of treating 1,060 patients with gonococcic infections by means of a single intramuscular injection of calcium penicillin-oil-beeswax are presented.

2. This method of therapy appears effective, safe, and widely applicable.

. The ability of this method to effect a
e does not appear related to sex, race,
failure of previous therapy.

4. This study was made possible only by the splendid cooperation of the following named participating physicians:

ctor Lewis Abramson,
30 Broadway,
Newport, R. I.

ctor O. L. Ader,
Durham County Health Officer,
Durham, N. C.

ctor James M. Alexander,
21 W. 7th St.,
Charlotte, N. C.

ctor James R. Amos,
Greene County Health Officer,
Greene County Health Department,
Springfield, Mo.

rgeon R. C. Arnold,
Venereal Disease Research Laboratory,
U. S. Marine Hospital,
Staten Island 4, N. Y.

nior Surgeon Alfred J. Aselmeyer,
U. S. Public Health Service
District No. 3,
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ptain Donald W. Atcheson, M. C.,
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State Board of Health,
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ctor Haynes Baird,
121 W. 7th Street,
Charlotte, N. C.

octor Daniel C. Barrett,
Sioux City, Iowa.

octor F. C. Beelman,
Executive Officer,
State Board of Health,
Topeka, Kans.

octor Ralph Behrend,
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octor E. A. Belden,
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octor H. D. Benwell,
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octor Walter L. Bierring,
Commissioner,
State Department of Health,
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octor DeWitt T. Boyd,
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Accelerated Methods of Treating Gonorrhea in the Female with Penicillin-wax-oil Mixtures

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The present standard methods of treating gonorrhea with penicillin dissolved in saline or distilled water have proved highly successful. However, the inconvenience of round-the-clock administration required by these methods is at once apparent, since hospitalization of the patient is necessary. From the viewpoint of the private practitioner, such a method leaves much to be desired; from a public health standpoint, it fails to achieve the objective of doing the most good for the greatest number. If the greatest number of infected patients is to be treated with penicillin, treatment methods requiring fewer injections are necessary. The aim is to obtain as nearly as possible a 100 percent cure with a minimum of inconvenience to the patients and personnel involved. The results thus far obtained are promising and are worthy of report at this time, for they confirm in principle the published and unpublished work of Romansky and Rittman (*1, 2*).

Penicillin, when administered intramuscularly in aqueous solution, is excreted rapidly in the urine. Injections every 2 to 3 hours are required for the most satisfactory results. The therapy for gonorrhea generally recommended at present consists of injections of 10,000 to 20,000 units every 3 hours for 6 to 8 doses, a total of 100,000 to 150,000 units over a period of 15 to 21 hours. Such a method, though yielding a high percentage of cure, does not permit widespread application to the problem of gonorrhea control. Methods are being evolved that may make penicillin therapy for gonococcic infections more readily adaptable for use in the treatment of outpatients both in clinics and in private practice.

In an effort to overcome the handicaps of

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round-the-clock administration of penicillin, various accelerated schedules have been tried. When a single intramuscular dose of 50,000 units in saline was given to a series of 10 patients, there were 80 percent failures (*3*). When a total of 100,000 units in saline divided in two doses 5 hours apart was tried in a series of 20 patients, failures were encountered in 45 percent (*3*). However, when Trumper and Hutter administered a single intramuscular injection of 50,000 units in saline into the deltoid region, chilling the site by icebags for 1 to 2 hours previous to the injection and for 6 to 12 hours afterwards, bacteriologic cures were obtained in 8 consecutive patients. These investigators claimed that continuous chilling applied at or around the site of the intramuscular injection retarded the circulation locally. The rate of absorption was thereby delayed so that bacteriostatic levels of penicillin were maintained in the blood for longer periods. This method appears too cumbersome to be practical for general use.

Van Slyke and Steinberg (*4*) used a schedule of treatment that could be completed in 7½ hours by giving 25,000 units in saline intramuscularly at 9:00 a.m., 11:30 a.m., and 2:00 p.m., and 50,000 units in a final treatment at 4:30 p.m. for a total dose of 125,000 units. This proved applicable for use in the outpatient clinic and yielded a cure rate of 84 percent. When a schedule of 4 injections of 16,000 units every 2½ hours during a period of 7½ hours was tried, to which a fifth injection was added the next morning for a total dose of 80,000 units, the cure rate was 87 percent. These schedules, though more convenient for both patient and personnel than the standard round-the-clock method, are still somewhat troublesome. Furthermore, the rate of cure is not as high as that obtained with other accelerated treatment schedules (table 1).

TABLE 1.—*Results, reported by various authors, of the treatment of gonorrhea by means of accelerated schedules employing penicillin in aqueous solution*

Investigator	Medium	Number of injections	Units per injection	Interval	Total dosage	Number of cases	Number of cures	Percentage of cure
Trumper and Hutter	Saline	1	50,000	—	50,000	10	2	20
	Saline	2	50,000	5 hours	100,000	20	11	55
	Saline	1 (Site chilled)	50,000	—	50,000	8	8	100
Thomas (unpublished)	Saline	3	50,000	2 hours	150,000	75	73	97
Van Slyke and Steinberg	Saline	4	3 of 25,000 4th 50,000	2½ hours	125,000	43	36	84
	Saline	5	16,000	2½ hours 5th injection 16 hours after 4th	80,000	93	81	87

Romansky and Rittman (*1*) have shown that the maintenance of demonstrable levels of penicillin in the blood may be prolonged by the use of a penicillin-beeswax-peanut oil mixture. Bacteriologic cures were obtained in 11 of 12 patients with gonorrhea by a single injection of 51,250 to 100,000 units suspended in 2 to 3 cc. of 0.75 to 3.0 percent beeswax in peanut oil. Stimulated by this contribution, we undertook an evaluation of several accelerated treatment schedules employing wax and oil for the treatment of gonorrhea in the female.

METHODS

This series is composed of white and Negro female patients who were institutionalized under moderately strict supervision. The diagnosis in every instance was estab-

ished bacteriologically in our laboratory after admission of the patient to the medical center. Secretions were obtained from the urethra and cervix and plated directly on chocolate agar (Difco) plates to which Difco supplement A had been added. The plates were incubated 48 hours at 35°C. in an atmosphere containing 10 percent carbon dioxide. The plates were inspected and sprayed with 1 percent para-aminodimethylaniline monohydrochloride. The oxidase positive colonies were picked, spread and stained by Hucker's modification of Gram's stain. A diagnosis of gonorrhea was made when gram-negative diplococci, morphologically resembling the gonococcus, were obtained from oxidase positive colonies.

After therapy a minimum number of 10 negative cultures were obtained over a period of 11 or more days, except for a few patients on whom only 5 to 8 cultures were done in 5 to 9 days. When cultures were positive after therapy, carbohydrate fermentation studies were made to ascertain that the organism under study was the gonococcus.

It must be noted that only the posttreatment cultures were confirmed by sugar fermentation tests, so that among the cases treated there may have been some patients not infected with gonococci. Therefore the failure rate may have been based on too large a number of cases.

MATERIALS

The sodium penicillin-2 percent beeswax-peanut oil mixtures used in the first part of this investigation were prepared essentially as outlined by Romansky and Rittman (*1*). In making our first mixture, we experienced considerable difficulty in obtaining powdered sodium penicillin in particles of uniform size and of even suspension. Homogenization was used in an attempt to standardize the suspension, the dispersion and possibly the absorption of the substances.

The chemical purity of our oil and beeswax was questionable, and after our first series of cases these substances were purified or fractionated. Our preparation designated mixture A, contained the fraction of beeswax soluble in boiling ethyl alcohol but insoluble in cold alcohol. This fraction, consisting of cerotic acid and its homologues, was incorporated with purified peanut oil to produce a viscosity comparable to that of 4 percent beeswax in peanut oil. Mixture B contained the fraction of beeswax insoluble after three extractions with moderate amounts of boiling ethyl alcohol. This fraction, usually referred to as myricin, is essentially myricyl palmitate and represents about 85 percent of the total weight of beeswax. It was incorporated with purified olive oil to yield a viscosity approximating that of an 8 percent beeswax-peanut oil mixture.

The methods used and the theoretical aspects concerning fractionation of the beeswax and purification of the oils need not be reported here. We have no information concerning the effect of homogenization upon the stability and absorption of penicillin.

No studies were made concerning the blood level of penicillin maintained or the amount of penicillin excreted in the urine during the use of any of our mixtures. The therapeutic efficacy of the mixtures was evaluated solely by the rate of cure.

It may be important to point out that most of the work of Romansky and Rittman has been with calcium penicillin. Sodium penicillin was used throughout the present study.

All mixtures were prepared by measuring the oil by volume and the wax, or wax fraction, by weight.

RESULTS

This study comprises 7 series of patients with whom different accelerated treatment schedules were employed. Simplification was attempted by the use of a single dose in a medium which would prolong the effective action of penicillin by maintaining a satisfactory bacteriostatic tissue fluid level over a sufficient period of time. Tables 2 and 3 outline the number of injections, the dosage, the interval of injections when 2 doses were employed, the medium in which the penicillin was dispersed, the total dosage, the number of cases in each series,

the number and the percentage of bacteriologic cures. Urethral and cervical secretions were obtained for culture over a minimal period of 11 or 12 days in the greater number of cases and a maximal period of 20 to 30 days in a lesser number of instances. When cultures were negative and clinical signs were present, smears were often examined for gonococci, and extra cultures were taken.

Of the 158 instances in which one or the other of the accelerated methods was used, employing 2 percent beeswax or mixture A, an over-all cure rate of 87 percent was obtained (table 2). The minimal number of cultures was 10 and the maximal was 20. Of the 20 failures, 18 (90 percent) occurred on or before the fifth culture. The exceptions were one who was first positive on the seventh and then again on the eleventh and twelfth cultures, and another which was positive on the tenth, eleventh, and twelfth cultures.

When sodium penicillin was suspended in mixture B and 150,000 units given as a single injection in the treatment of 61 female patients (table 3), all were cured except one (98.4 percent). This result closely approaches that reported by Romansky and Rittman (*2*) and Thomas (*5*). Romansky and Rittman used a single injection of 150,000 units of calcium penicillin in 4 percent beeswax-peanut oil mixture to cure all in a series of 80 males. Their series was later extended to 150 patients without a single failure (*2*). When injections of only 100,000 units of this mixture were employed, the rate of cure was 93 percent. Thomas (*5*) evaluated the efficacy of this mixture in 47 women and obtained cures in 46 (98 percent) after a single injection of 150,000 units.

TABLE 2.—*Results of the treatment of gonorrhea by means of accelerated schedules employing penicillin in 2 percent beeswax-peanut oil and in mixture A*

Number of injections	Units per injection	Interval	Medium	Total dosage	Number of cases	Number of cures	Percentage of cure
2.....	50,000	5 hours	2 percent beeswax peanut oil mixture	100,000	56	51	91
1.....	100,000	—	2 percent beeswax peanut oil mixture	100,000	49	40	82
1.....	50,000	—	2 percent beeswax peanut oil mixture	50,000	17	15	88
2.....	50,000	24 hours	Mixture A (homogenized)	100,000	26	24	92
1.....	150,000	—	Mixture A (homogenized)	150,000	10	8	80
				Total...	158	138	87

TABLE 3.—*Results of the treatment of gonorrhea by means of a single injection of penicillin in mixture B (myricin and purified olive oil)*

Number of injections	Dosage	Medium	Number of cases	Number of cures	Percentage of cure
1.....	150,000	Mixture B (homogenized)	20	20	100
1.....	150,000	Mixture B	41	40	97.6
		Total.....	61	60	98.4

It is of interest to note that Romansky and Rittman felt that the calcium salt of penicillin should be used (since it is less hygroscopic and more uniformly dispersed than the sodium salt) and that the beeswax concentration should not exceed 4 percent. In our series, the sodium salt of penicillin was used, and mixture B had a viscosity equivalent to an 8 percent beeswax-peanut oil mixture. In spite of these departures from the original technic, our mixture yielded 98.4 percent of bacteriologic cures. It should be pointed out, however, that in our series massage at the site of injection was practiced for a period of a few seconds or minutes. It is now believed advisable to avoid massage so as not to interfere with delay in penicillin absorption. Although penicillin blood levels were not determined in our cases, our empiric choice of a mixture of such a high viscosity resulted in a high percentage of cures. Further investigations are being carried on to determine whether lower percentages of our mixture B will prove as efficacious as the more viscid mixture used in this study. Although beeswax has proved highly effective in prolonging the action of the penicillin, it is possible that certain fractions of beeswax may prove more useful because they are definite compounds and may more readily be standardized.

Penicillin resistance was not encountered in a single case. All but one patient, who failed on the first course, responded to a second course of therapy with the standard or another accelerated method. This patient, after failing with two courses, responded to a third course of therapy. There has been no definite evidence of allergic manifestations attributable to penicillin, beeswax or beeswax fractions, in any of our treatment schedules.

The question arises—how many posttreatment cultures are required for test of cure?

In our two groups of cases, one comprising 158 patients with 20 failures (table 2), and the other 61 patients with a single failure (table 3), there was a total of 21 failures among 219 patients. Of these failures, 4 were detected by culture examination on the first day after therapy, 7 on the second day, 3 on the third day, 2 on the fourth day, and 2 on the fifth day. Only 3 were detected between the sixth and nineteenth days (table 4).

TABLE 4.—*Results of cultures taken on 21 cases of treatment failure*

Cases	Cultures														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1.....	−	+	+	−	+	+	−	+	+	+					
2.....	−	−	−	+	−	−	−	−	−	−	−	−	−	−	+
3.....	+	+	+	+											
4.....	−	−	−	−	+	+	+								
5.....	+	−	+	+											
6.....	+	−	+	+	+	+									
7.....	−	+	+	+	+										
8.....	−	−	+	−	+	+									
9.....	−	+	+	−	+	+									
10.....	−	+	+	+											
11.....	−	+	+	+	−	+	+	+							
12.....	−	−	−	−	+	−	−	−	+	−	+				
13.....	−	−	−	−	−	−	+	—	−	−	+	+			
14.....	−	−	+	+	+										
15.....	−	+	+	−	−	−	+	+	+						
16.....	−	−	−	−	−	−	−	−	−	+	+	+			
17.....	−	−	+	+	+	+									
18.....	+	+	+	+											
19.....	−	+	+	+	+										
20.....	−	−	−	+	+										
21.....	−	−	−	−	−	−	−	+	+	+					
Failures.....	4	7	3	2	2		1	1		1					

Therefore, if it could be assumed that following penicillin treatment no asymptomatic carrier states occur which may later become active infections, it could be said that only 14 percent of the failures would be missed by the use of 5 negative cultures as a criterion of cure. This would constitute 1.4 percent of the patients in our whole series, and considering only the results following the treatment schedule of a single injection of 150,000 units of penicillin in 4 percent beeswax-peanut oil mixture (*2*) or in our mixture B, only 0.2 percent of the patients treated would be missed as treatment failures. Further work is needed to determine whether or not relapses occur and whether they can be detected several weeks after treatment with or without the use of provocative procedures.

DISCUSSION

It appears evident that the degree of prolongation of absorption is dependent upon the amount of wax substance suspended in an oil (*1*). We were aware of the fact that Romansky and Rittman were not able to demonstrate penicillin in the blood following the use of a 5 percent beeswax-peanut oil mixture. By analogy, our mixture B having a viscosity comparable to that of 8 percent beeswax in peanut oil probably would not yield a demonstrable level of penicillin in the blood. Our results do not indicate that demonstrable blood penicillin levels as determined by present methods are a requisite for the satisfactory treatment of gonorrhea with penicillin. Theoretically, absorption can be retarded to such a degree that the penicillin will be ineffective. This does not seem possible with suspensions of wax in oil because of the great difficulties attendant upon the intramuscular injection of mixtures having a viscosity greater than that of 8 percent beeswax in oil.

CONCLUSIONS

1. The development of an accelerated method of treating gonorrhea with a single injection of penicillin is highly desirable. It will implement a mass attack on the problem of the treatment of gonorrhea in the offices of physicians in private practice, or in clinics throughout the country.

2. The results of treatment of gonococcic infections by the use of one or two injections of a mixture of penicillin in substances which delay absorption have been very encouraging.

3. Bacteriologic cures were obtained in 87 percent of our first group of 158 women treated with one or two injections of sodium penicillin incorporated in various wax-oil mixtures.

4. Bacteriologic cures were obtained in 98.4 percent of our second group of 61 women treated with a single intramuscular injection of 150,000 units of sodium penicillin in a vehicle containing a beeswax fraction in purified oil having a viscosity equivalent to an 8 percent beeswax-peanut oil mixture. The beeswax fraction is that obtained after three extractions with moderate amounts of boiling ethyl alcohol.

5. The results substantiate the work of Romansky and Rittman who employed 150,000 units of calcium penicillin in 4 percent beeswax-peanut oil mixture with 100 percent cures in 150 male patients.

6. Further investigations are being carried on to determine whether lower percentages of our mixture B will prove as efficacious as the more viscid mixture used in this study. Although 4 percent beeswax has proved highly effective in prolonging the action of the penicillin, it may be that certain fractions of beeswax will prove more acceptable because they may more readily be standardized.

7. The criteria of cure in this study consisted for the greater part of 10 daily negative cultures taken from the cervix and urethra over a minimum of 11 days.

8. Neither penicillin resistance nor allergic sensitivity was encountered in any of our patients.

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ADDENDUM

Since this paper was prepared, a group of 92 women has been treated with a myricin-peanut oil mixture having a viscosity approximating that of 4 percent beeswax in peanut oil. Penicillin was added so that the resulting suspension contained 75,000 units per cubic centimeter. Each patient received a single injection of this mixture containing 150,000 units. Of this group, 87 (94.6 percent) patients responded favorably to treatment.

Rubber diaphragm capped bottles containing an amount of the mixture sufficient to treat 25 patients were prepared as needed. A small amount of water was accidently introduced into one of these. This resulted in a separation of aqueous penicillin. Three of the 5 failures occurred in patients who were treated with this particular lot of wax and oil mixture.

DIAGNOSIS

Syphilitic aortitis and aneurysm. Aaron Arkin. M. Clinics North America, Philadelphia, pp. 70–85, Jan. 1944.

The author discusses in considerable detail the pathology and diagnosis of cardiovascular syphilis, with emphasis on methods for the early diagnosis of uncomplicated syphilitic aortitis.

Aortic regurgitation is perhaps the most important pathologic change in syphilitic heart disease. Pulmonary regurgitation may rarely occur. Another important change is stenosis of the ostia of the coronary arteries, which is a part of the aortitis in the sinuses of Valsalva and which leads to angina pectoris and not uncommonly to sudden death.

The most common symptom of aneurysm is pain, usually due to erosion of bony structures or pressure on nerve trunks. Dyspnea, cough, dysphagia and hoarseness, in that order of frequency, are the next most common symptoms. Visible pulsation, tracheal tug, and pulsus differens are signs frequently encountered. The radiographic diagnosis is, of course, essential.

The earliest and most important diagnostic sign of syphilitic aortitis is a widening of any part of the aorta seen at fluoroscopic examination. Other findings, in order of their importance, are increased manubrial dullness, especially on the right, tambour or bell-like, ringing, aortic second sound, systolic murmur at the base, pulsus differens, angina pectoris, and suprasternal pulsation.

The author concludes with a brief discussion of the differential diagnosis between syphilitic and rheumatic aortic regurgitation.

Malaria and the serological reactions for syphilis in British soldiers. B. G. T. Elmes and G. M. Findlay. J. Roy. Army M. Corps, London, **84**: 29–30, Jan. 1945.

This study was undertaken to determine whether British soldiers having no history of syphilis but suffering from malaria who are resident in a hyperendemic malaria region would show a positive reaction when examined by the standard Kahn test.

The patients were 80 soldiers with malignant tertian malaria, who had not been more than 18 months in the malarial zone and who had no previous history of syphilitic infection. They were given the Kahn test usually within 24 hours of the demonstration of P. falciparum in the blood. Ide tests were carried out at the same time.

Of all the patients tested, 23 showed a positive Kahn reaction, but only 4 showed a positive response to the Ide test. No case exhibited a positive Ide and a negative Kahn reaction. Eliminating the 1 case which showed evidence of syphilis, 22 of the 79 patients (27.0 percent) at

some period showed a positive Kahn reaction. In most cases, this reaction was temporary, but in some, it was still present 42 days after the first demonstration of parasites in the peripheral blood.

TREATMENT

Oral administration of penicillin in oil. Raymond L. Libby. Science, Lancaster, 101: 178–180, Feb. 16, 1945.

This paper presents the author's investigation of an oil-and-penicillin solution for the oral administration of penicillin in experimental animals and in human patients.

Sodium and calcium salts of penicillin in cottonseed oil suspensions were administered in capsules. A single oral dose of 90,000 units maintained the penicillin level in the blood at or about 0.03 units per cc. for at least 4 hours in a human patient. An initial oral dose of 90,000 units of penicillin followed by 2 subsequent doses of 20,000 units given 3 and 6 hours later, respectively, maintained the drug at this level for 7 hours with only a slight decrease at the eighth hour. It was found that optimum blood levels were obtained by giving the dose on an empty stomach, since gastric acidity probably inactivates a portion of the drug.

According to these preliminary results, a greater amount of penicillin may be required in the oral administration of penicillin than in the administration by other routes, but this disadvantage is offset by the greater ease of medication to both physician and patient. Furthermore, less highly refined penicillin is required in oral administration than in injections.

Prolongation of the action of penicillin after intramuscular injection. Charles D. Armstrong, Richard M. Halpern and Windsor C. Cutting. Proc. Soc. Exper. Biol. & Med., Utica, 58: 74–76, Jan. 1945.

In an attempt to obtain a more satisfactory prolongation of the residence of penicillin in the body, the authors experimented with various agents in dogs and in man.

Preliminary experiments with 15 different agents were made on dogs, and on the basis of these, penicillin in dextrose alone and in a combination of dextrose with a vasoconstrictor was administered to patients and normal human beings. Thirty-nine sets of observations were made on 12 patients. The concentration of penicillin was 5,000 units per cc., and a 5 percent solution of dextrose was used. Dextrose appeared to furnish a satisfactory and harmless extension of the action of the drug which was of sufficient extent to be of clinical value when large doses of penicillin are used. Unlike the low blood concentrations produced by mixtures of penicillin with peanut oil and beeswax, the dextrose solution gives a high concentration of penicillin in the blood immediately after injection, and no foreign substance remains in the tissues. The authors suggest that a continuous concentration of the drug at a low level may be more effective therapeutically than separated spikes of higher concentration.

The treatment of primary and secondary yaws with penicillin. A preliminary report. Richard Whitehill and Robert Austrian. Bull. Johns Hopkins Hosp., Baltimore, 75: 232–240, Oct. 1944.

Findings are reported in the penicillin treatment of 17 patients with primary and secondary yaws from which Treponema pertenue was isolated by darkfield examination. Eleven of the patients had received no previous arsenical treatment, and 6 patients with active yaws had a history of clinical relapse following previous chemotherapy. Penicillin was administered intramuscularly in doses of 15,000 units at 4-hour intervals for 5 or 6 days. Kahn reactions were determined during and after hospitalization at weekly intervals.

In 16 patients, T. pertenue disappeared from the cutaneous lesions within 16 hours and in 1 patient within 40 hours. Within 3 weeks, all cutaneous manifestations of the disease had healed with the exception

of 1 lesion which became surrounded with scar tissue. During the 7-week observation period, penicillin did not significantly affect the serum Kahn reaction.

The authors comment that the clinical importance of a positive serologic test in yaws may have a different significance than in syphilis, although one of the criteria of a complete cure of yaws is a permanent negative serologic reaction.

Artificial fever-chemotherapy. III Charting procedures. G. X. Schwemlein, H. Worley Kendell and R. M. Craig. Arch. Phys. Med., Chicago, 26: 8–19, Jan. 1945.

This article describes a system of charting which presents a summary of the patient's treatment status taken at 15-minute intervals. The charts were developed at the Chicago Intensive Treatment Center during the treatment of 1,667 patients with fever chemotherapy for early syphilis.

In the fever therapy department, a nurse-technician under a physician's supervision is responsible for the administration to each patient of an 8-hour session of physically induced fever at 106.0°F. and of concomitant doses of mapharsen. By means of the chart here described, the physician has for ready reference data taken every 15 minutes on each patient under treatment. The following points are included: rectal temperature, blood pressure, specific gravity of the blood plasma, emesis, oral and parenteral fluids, urine, oxygen, rheostat readings, humidity of the cabinet, room temperature, and medication.

The authors have found such a record a practical means of compiling statistical data and imperative for the safety of the patient when 6 or 8 cases are being treated simultaneously.

Inhibition of drug precipitation in the urinary tract by the use of sulfonamide mixtures. I. Sulfathiazole-sulfadiazine mixture. David Lehr. Proc. Soc. Exper. Biol. & Med., Utica, 58: 11–14, Jan. 1945.

The present investigation deals with the possibility of lessening the danger of renal concrement formation by the employment of sulfonamide mixtures.

Solubility studies showed that N^1-heterocyclic derivatives of sulfanilamide are soluble in one and the same solution nearly to the extent of their separate solubilities. Since closely related sulfonamides present in the same solution do not influence each other appreciably with regard to their particular solubilities, the danger of intrarenal drug precipitation from the sulfonamides comprising the mixture should be only as great as if each compound had been administered alone, and in the partial dosage contained in the mixture. And the use of a combination of different sulfonamides having similar therapeutic indications should produce an antibacterial effect corresponding to the total concentration of free sulfonamide.

To test the validity of these ideas, intraperitoneal injections of sulfadiazine, of sulfathiazole, and of a mixture of the 2 drugs were given to albino rats, and in vitro studies of the antibacterial efficacy of solutions containing equal parts of the 2 drugs against strains of streptococcus and pneumococcus were made.

Results of these experiments showed that the acute and chronic toxicity of the drug combination for albino rats is strikingly low as compared with the effect of similar total concentrations of either drug alone. Evidence derived from chemical analyses and postmortem examinations pointed to a diminution of intrarenal obstruction from drug precipitate as the chief reason for the low toxicity of the mixture. In vitro antibacterial studies showed that the effectiveness of the mixture corresponded largely to the total concentration of free sulfonamide.

The author concludes that the administration of doses of a combination of sulfathiazole and sulfadiazine instead of either drug alone would decrease the danger of renal complications in patients without lessening the antibacterial effect of the treatment. Clinical trials are in progress.

LABORATORY RESEARCH

The serological diagnosis of syphilis. Hans Neurath, E. Volkin, J. O. Ericksen, F. W. Putnam, H. W. Craig, G. R. Cooper, D. G. Sharp, A. R. Taylor and J. W. Beard. Science, Lancaster, **101**: 68–69., Jan. 19, 1945.

The results of an investigation directed toward the development of a serodiagnostic method for differentiating between true syphilitic and biologic false positive serums are the subject of this report.

A total of about 300 syphilitic and biologic false positive serums were used in investigating the various phenomena described. The approach to the problem was based on nonspecific methods of characterization and fractionation of the serums as follows: electrophoresis, fractionation, inhibition and redispersion, heat stability, and adsorption on calcium phosphate.

The observations described indicated that the antibodies of truly syphilitic serums, reactive with lipoidal antigen, differ from those of biologic false positive serums in certain chemical and immunologic respects. The possibility of the application of these findings to the development of a practical method of differentiation is being explored.

The in vitro tolerance of the gonococcus for penicillin. Charles E. Lankford. Am. J. Syph., Gonor. & Ven. Dis., St. Louis, **29**: 56–63, Jan. 1945.

In the present investigation, 203 freshly-isolated gonococcic cultures from 100 female patients were tested for in vitro penicillin tolerance. Simultaneous tests of each strain for its sulfathiazole tolerance were performed. The method used, a relatively simple, semiquantitative one, is described.

In agreement with the results of Cohn and Seije, the author found no naturally resistant strain of gonococcus. The extremes of tolerance of the organism for penicillin observed in both studies were almost identical: 0.0025 to 0.02 O. u. per milliliter, with the median falling between 0.0075 and 0.01 O. u. per milliliter, a relatively narrow range of tolerance as compared with the very wide range of the tolerance of the gonococcus for sulfonamide. Neither study, however, according to the present author, provides a basis for conclusions regarding the possibility of acquired penicillin resistance.

No correlation of in vitro tolerance of penicillin and sulfathiazole was demonstrated.

The use of a solid medium for the transportation of specimens for gonococcus culture. Nell Hirschberg. Am. J. Syph., Gonor. & Ven. Dis., St. Louis, **29**: 64–70, Jan. 1945.

Experience in the use of solid medium for the transportation of specimens for gonococcus culture, its introduction as a routine procedure in the State of North Carolina, and further experiments with the composition of this medium, recently developed by the author, are reported in this paper.

The medium and the method of its preparation are described, and mention is made of the continued search for a suitable inhibitor of contaminants, Nile blue A being the most satisfactory one so far tried. Additional experiments on the composition of the medium are in progress.

Delayed cultures were made from 2 series of specimens grown on the medium, the first consisting of 187 specimens, the second of 31. All gonococci isolated in the first series were identified by sugar fermentation tests. The results observed in these delayed cultures were checked against those made in immediate cultures from the same specimens.

The medium, which has been made available to physicians in the State, has been tested in all kinds of weather, withstands transportation well, and isolates a sufficient number of the gonococci to render its use desirable, particularly where local laboratory service is not available.

An etiologic consideration of Donovania granulomatis cultivated from granuloma inguinale (three cases) in embryonic yolk. Katherine Anderson, W. A. DeMonbreun and E. W. Goodpasture. J. Exper. Med., Baltimore, **81**: 25–38, Jan. 1945.

In a previous report Anderson very briefly described the successful cultivation in the yolk of living chick embryos of an organism having all the morphologic characteristics of Donovan bodies. The present paper describes in greater detail continued observations on the original and two additional strains isolated from patients with granuloma inguinale. The authors describe in detail the technics of isolation and culture. The morphology and cultural characteristics are discussed, and immunologic evidence is presented to support the view that the organism is in fact the etiologic agent of granuloma inguinale.

The authors' summary follows:

1. This organism has been cultivated in vitro only in media containing embryonic yolk. It failed to grow on any of a variety of artificial media.

2. It has not proved to be pathogenic for common experimental animals.

3. The Donovan body is reproduced in the epithelial cells of the yolk sac and in the yolk. The microorganism evidently reproduces both extracellularly and intracellularly.

4. The microorganism produces, in culture, antigens that elicit immune reactions in the skin and serum of granuloma inguinale patients.

5. This microorganism is judged to be a bacterium and the etiologic agent of granuloma inguinale.

6. It is proposed that these strains of the bacterium be the type of a new genus, *Donovania*, in recognition of Donovan's original description of the pathognomonic bodies of granuloma inguinale; and that the specific name granulomatis be applied to designate its relationship to the characteristic lesion of the disease.

Immunologic relationship of Donovania granulomatis to granuloma inguinale. Katherine Anderson, E. W. Goodpasture and W. A. DeMonbreun. J. Exper. Med., Baltimore, **81**: 41–50, Jan. 1945.

This paper reports additional experiments carried out for the purposes of investigating the etiologic relationship between the Donovania granulomatis and granuloma inguinale in the human patient, and determining the specific antigenic relationship between that organism cultivated in embryonic chick yolk and the cutaneous tissue of patients with active lesions of granuloma inguinale.

The methods and material used are described and the authors' interpretation of the results is discussed.

A washed bacterial suspension of Donovan microorganisms cultivated in the yolk of chick embryos was used as an antigen in intracutaneous tests in 6 cases of granuloma inguinale in the active stage of the disease. These injections were responded to by an extensive erythematous and edematous reaction that reached its height in 24 hours and disappeared within 48 hours. Four control cases without granuloma inguinale showed only as much reaction to the injection as was to be expected from the slight trauma incident to it. The skin of the reacting patients responded in a similar manner but to a lesser extent to a filtrate of infected yolk. Simultaneous control injections of filtered normal yolk demonstrated that sensitivity to normal yolk was not responsible for the reactions.

A mucoid material present in infected yolk, considered to be of capsular origin, injected intradermally into patients with active granuloma inguinale elicited a milder reaction, but one considered to be specific.

The capsular material in suitable dilution elicited distinct precipitation reactions when mixed with the serum from 18 of 19 patients with active granuloma inguinale. Serum from 1 active case showed no precipitation. Sixty-four serums including 6

from lymphogranuloma venereum patients and 18 from Wassermann- or Kahn-positive patients, and 1 from an early chancroid failed to precipitate. Two serums from a total of 66 used as controls showed a precipitate in the presence of the capsular material. These patients gave no history or evidence of granuloma inguinale.

The capsular material fixed complement in the presence of serum from patients with granuloma inguinale. Serum from 12 of 15 patients with granuloma inguinale demonstrated complement fixation. Three failed to fix complement. Of 19 control serums 18 failed to fix complement in the presence of capsular material and 1 fixed only a very slight amount of complement. None of these serums nor the capsular material itself was anticomplementary.

The authors conclude that the high proportion of precipitation and complement fixation reactions obtained from patients with active granuloma inguinale is indicative of a specific immunologic relationship of the Donovan microorganism cultivated in embryonic yolk to the disease, granuloma inguinale. They are of the opinion that one or all of the methods described may eventually be so standardized as to be of distinct diagnostic value.

PUBLIC HEALTH ADMINISTRATION

Venereal diseases among the migrant farm laborers of New Jersey. Glenn S. Usher and Henry Cowan. J. M. Soc. New Jersey, Trenton, **42**: 11–14, Jan. 1945.

This paper reports the experience of the New Jersey State Department of Health with the venereal disease problem among migrant farm workers in Monmouth, Mercer, and Middlesex Counties.

In the initial attempt at control, examining teams went to the farms to collect blood specimens, and patients with positive reactions were sent to health department clinics for treatment. Since this plan proved unsatisfactory, seasonal clinics operated by the bureau were tried, and farmers were urged to demand a card from each employee indicating that he had reported to the clinic. One-fourth of the migrant workers was the maximum number reached by this plan. The success of the work was limited by the short duration of the season, the difficulty of follow-up as workers move from farm to farm, and the difficulty of referring them to treatment sources near their homes for continued treatment.

In 1944, efforts were directed toward two objectives: obtaining the cooperation of the farmers and the finding of infectious cases, treatment of which could be completed during the summer by the use of penicillin. But in spite of intensive efforts, most farmers remained apathetic, and only 756 of the approximate 2,800 workers in the area were examined.

Examinations given included blood tests, inspections for lesions and for evidence of gonorrhea, darkfield, and in the case of women, gonococcus cultures confirmed by sugar fermentations. The results are tabulated, showing the incidence of infection among men, women, and in both sexes in various age groups.

The authors summarize their findings as follows:

1. The venereal disease rate was found to be very high. In women between the ages of 15 and 24 years, 6.3 percent of those examined were found to have darkfield positive lesions, and 30.6 percent were found to have gonorrhea.

2. Most of these infections were imported to New Jersey. They are a hazard to the people of the areas traversed and to those of New Jersey.

3. The living conditions of these workers favor the spread of the diseases. They are in urgent need of correction.

4. Routine medical examination of all migrant workers and prompt application of rapid treatment methods are needed. Legislation to require such examinations and perhaps enforcement of the interstate quarantine law would be helpful.

New Cases of Syphilis and Gonorrhea in States, Territories and Possessions

Health officers' monthly statement: Reported for the first 7 months of fiscal years 1944-45 and 1943-44

Area	Cases of syphilis and gonorrhea reported for first 7 months of fiscal years below:											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44
Total†	[1]197,696	[1]266,367	[1]41,773	[1]43,938	[1]54,206	[1]70,335	[1]80,918	[1]117,370	[1]6,738	[1]7,737	[1]155,168	[1]173,413
Alabama.....	7,488	10,157	1,071	1,448	1,600	2,338	1,530	2,446	167	219	3,813	3,848
Arizona.....	1,052	1,653	317	392	321	442	321	643	81	71	659	1,038
Arkansas.....	6,568	5,759	1,580	703	2,210	1,932	2,225	2,191	196	134	3,754	2,651
California.....	16,601	18,401	3,048	3,041	3,756	4,339	8,997	10,115	501	553	17,869	19,503
Colorado.....	1,540	2,520	417	609	456	713	612	1,096	55	102	1,349	1,993
Connecticut....	1,390	1,727	140	213	650	710	285	480	45	71	667	910
Delaware.....	351	529	85	61	104	128	129	107	14	8	124	112
Dist. Columbia.	2,357	4,663	543	543	724	1,127	929	2,770	59	81	3,062	2,147
Florida.....	9,303	17,085	1,157	1,926	3,417	5,327	3,913	7,775	251	346	7,511	9,813
Georgia.....	6,158	9,320	1,725	1,838	2,464	3,726	1,787	3,484	179	268	4,619	6,277
Idaho.....	494	338	93	160	126	59	246	93	19	5	263	503
Illinois.....	12,749	16,212	2,193	2,126	3,038	3,755	7,157	10,019	361	312	12,020	13,702
Indiana.....	3,631	4,943	755	743	481	460	1,227	1,799	118	134	1,645	2,030
Iowa.....	934	1,417	220	285	270	367	369	612	41	98	1,397	1,055
Kansas.....	1,548	1,618	384	335	270	325	834	896	60	62	1,494	1,135
Kentucky.....	3,048	4,202	775	618	697	915	1,104	1,794	147	171	2,824	2,076
Louisiana.....	6,384	10,762	1,474	1,747	1,941	2,796	1,557	2,820	257	274	6,089	7,996
Maine.....	480	460	93	111	57	59	207	219	36	38	954	772
Maryland.....	4,685	9,172	982	987	1,160	937	1,218	1,629	101	72	2,726	4,461
Massachusetts..	2,392	3,269	568	670	(§)	(§)	1,700	2,404	124	193	2,423	2,968
Michigan.....	9,844	9,945	1,785	1,445	2,761	2,583	3,625	4,193	246	254	6,855	6,450
Minnesota.....	1,162	1,418	178	134	107	139	797	1,051	46	64	1,374	1,141
Mississippi.....	11,743	15,191	4,025	5,156	3,433	4,279	3,646	5,147	639	605	17,455	17,410
Missouri.....	5,318	6,001	1,180	1,033	1,482	1,545	2,292	2,869	181	197	4,678	3,345
Montana.....	254	242	51	66	21	41	70	98	6	5	174	192
Nebraska.....	804	749	126	117	222	368	411	210	31	23	886	903
Nevada.....	208	450	58	15	1	81	77	312	7	17	396	227
New Hampshire	165	139	17	18	31	32	101	77	12	6	97	115
New Jersey....	4,724	6,476	710	775	1,263	2,019	2,486	3,403	205	263	2,666	3,132
New Mexico...	993	1,142	214	245	276	259	448	582	69	56	726	843
New York.....	18,416	21,726	3,734	3,231	3,851	3,721	10,170	13,895	484	609	8,629	11,451
North Carolina.	(*)	6,580	(*)	1,700	(*)	2,641	(*)	2,124	(*)	115	(*)	5,273
North Dakota..	123	175	26	61	17	29	49	51	7	10	199	160
Ohio.....	11,109	13,371	2,368	2,061	3,034	3,174	5,248	6,820	459	535	3,759	3,103
Oklahoma.....	4,429	4,632	696	607	1,129	1,326	1,427	1,708	147	172	4,637	2,927
Oregon.....	1,139	1,206	313	364	130	99	643	707	43	36	1,450	1,518
Pennsylvania...	6,432	7,743	1,186	1,023	2,133	2,983	2,069	2,824	273	385	0	614
Rhode Island...	506	643	112	48	48	68	251	463	21	15	799	444
South Carolina.	4,640	9,236	1,349	1,922	1,513	3,714	1,434	3,156	177	228	3,905	3,906
South Dakota..	241	282	38	58	67	42	106	134	25	25	283	239
Tennessee.....	7,811	10,879	1,337	1,425	2,984	4,433	3,042	4,668	263	242	6,914	8,810
Texas.....	7,799	15,034	1,702	1,819	2,731	4,509	2,623	6,156	287	424	5,031	6,370
Utah.....	329	530	97	134	33	71	190	313	9	12	310	380
Vermont.....	102	150	14	51	29	43	41	49	10	7	231	109
Virginia.....	5,374	8,616	1,619	2,478	2,177	3,281	1,369	2,560	151	163	3,221	7,327
Washington....	2,196	2,619	477	532	511	577	893	1,148	45	83	2,957	5,225
West Virginia..	1,274	2,212	493	396	186	353	288	533	37	66	1,530	1,331
Wisconsin.....	504	558	119	105	3	0	371	447	11	6	628	647
Wyoming.....	910	795	129	63	291	111	404	404	35	17	116	104
Territories, Possessions												
Canal Zone....	478	(*)	61	(*)	97	(*)	266	(*)	15	(*)	316	(*)
Alaska.....	57	58	21	32	12	13	14	10	1	1	282	266
Hawaii.....	381	506	98	92	49	63	206	363	20	27	743	974
Puerto Rico....	6,069	9,316	875	964	2,090	1,886	1,688	3,082	1,313	1,166	3,513	2,385
Virgin Islands..	137	127	31	25	78	76	21	20	2	6	53	211
Actual total#, U. S. and Possessions.....	204,818	282,954	42,859	46,751	56,532	75,014	83,113	122,969	8,089	9,052	160,075	182,522

*No data available.
**Includes "not stated."
†Based on States reporting in both fiscal periods.
#Includes all reported cases.
§Included in late latent.
[1]Based on 47 States and District of Columbia.

New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over

Health officers' monthly statement: Reported for the first 7 months of fiscal years 1944-45 and 1943-44

City	Cases of syphilis and gonorrhea reported for first 7 months of fiscal years below:											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44
Total†	[1]13,743	[1]96,954	[2]14,577	[2]11,058	[2]17,490	[2]20,980	[2]33,297	[2]43,078	[2]1,817	[2]1,772	[1]53,902	[1]45,934
Akron	555	532	139	72	128	133	255	298	33	29	380	204
Atlanta	1,518	1,613	421	423	442	508	625	774	30	19	1,741	760
Baltimore	3,212	7,349	822	760	833	673	1,036	1,266	44	40	1,759	1,744
Birmingham	1,626	2,750	224	193	410	799	430	700	44	51	435	369
Boston	872	1,061	203	210	80	0	468	682	33	29	886	772
Buffalo	1,002	1,198	157	143	139	141	673	883	33	31	662	521
Chicago	8,831	9,020	1,621	1,430	2,243	2,162	4,756	5,258	211	170	8,338	7,660
Cincinnati	1,372	1,839	233	244	0	0	1,139	1,595	0	0	657	566
Cleveland	2,444	2,359	487	437	785	752	1,122	1,113	50	57	1,061	858
Columbus	809	874	253	174	181	189	343	467	32	24	263	182
Dallas	(*)	1,472	(*)	266	(*)	303	(*)	892	(*)	10	(*)	437
Dayton	620	1,038	77	118	223	295	300	592	20	33	322	433
Denver	(*)	1,228	(*)	275	(*)	318	(*)	464	(*)	38	(*)	1,092
Detroit	5,729	7,014	1,179	905	1,997	2,172	2,442	3,816	111	121	3,290	3,401
Honolulu	145	261	30	40	19	37	84	165	7	19	521	667
Houston	978	1,123	219	183	371	395	348	511	40	34	1,193	1,331
Indianapolis	1,129	1,276	220	339	142	37	269	290	17	16	380	64
Jersey City	222	308	25	31	70	65	114	204	13	18	46	27
Kansas City	818	1,058	161	178	194	194	407	644	35	40	618	564
Los Angeles	6,108	6,531	1,652	0	399	2,629	3,875	3,724	182	178	3,977	2,917
Louisville	767	1,232	250	189	157	217	312	517	21	13	901	518
Memphis	3,373	3,881	454	328	1,589	1,842	1,197	1,656	133	55	3,024	3,298
Milwaukee	329	291	55	30	12	4	258	243	5	1	235	107
Minneapolis	336	398	82	62	56	61	188	265	10	8	639	474
Newark	1,023	1,347	201	168	337	349	468	789	27	41	731	521
New Orleans	834	1,772	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,027	1,317
New York	13,269	15,031	3,031	2,688	3,310	3,329	6,500	8,464	319	369	8,629	8,199
Oakland	1,005	919	141	104	263	225	510	554	28	26	1,155	793
Oklahoma City	(*)	1,191	(*)	116	(*)	329	(*)	380	(*)	23	(*)	559
Omaha	319	335	62	30	71	189	178	91	8	18	273	297
Philadelphia	3,505	5,955	455	203	701	716	949	762	97	52	657	534
Pittsburgh	877	5,310	161	(*)	233	(*)	430	(*)	53	(*)	199	63
Portland	(*)	523	(*)	137	(*)	33	(*)	345	(*)	8	(*)	601
Providence	260	317	27	52	32	28	148	207	10	6	113	104
Rochester	177	157	38	31	12	13	124	110	3	3	249	173
St. Louis	3,389	3,517	699	454	1,070	1,191	1,520	1,754	100	108	2,466	1,116
St. Paul	143	173	20	20	23	30	80	111	8	5	160	178
San Antonio	(*)	697	(*)	93	(*)	191	(*)	384	(*)	24	(*)	816
San Diego	710	724	112	67	209	210	294	392	28	26	663	533
San Francisco	1,504	1,751	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,642	1,273
Seattle	878	808	195	103	223	143	441	510	12	14	1,170	979
Syracuse	373	605	40	17	14	20	279	551	5	17	272	190
Toledo	325	564	49	89	31	105	236	350	9	20	106	80
Washington, D C.	2,357	4,663	543	543	724	1,127	929	2,770	59	81	3,062	2,147
Actual total‡	73,743	102,065	14,738	11,945	17,723	22,154	33,727	45,543	1,870	1,875	53,902	49,439

*Data not available.
**Includes "not stated."
†Based on cities reporting in both fiscal periods.
‡Includes all reported cases.
[1]Based on 39 cities.
[2]Based on 36 cities.

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UNITED STATES PUBLIC HEALTH SERVICE

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Venereal Disease Case Finding

Recent years have witnessed remarkable advances in the treatment of venereal diseases. However, neither society nor individuals will derive appreciable benefit unless these advances in medical science can be applied to infected persons early in the course of their disease. Each year a large number of persons are infected with syphilis but do not begin treatment until the latent or late stages, if at all. The proportion of the total cases of gonorrhea coming to treatment cannot be estimated but is probably less than that of syphilis. It is obvious, therefore, that more effort must be expended on case finding.

The three principal case-finding methods, education, routine examination and contact tracing, are discussed in three papers in this issue. Education is shown in two of the papers to be an effective means for bringing large numbers of persons to voluntary treatment. In primary and secondary syphilis, gonorrhea and other venereal diseases, it leads all other methods of case finding. As might be expected, routine or screening tests bring in the bulk of the latent (symptomless) syphilis. However, a physical examination given in connection with the blood test can have great value as a means of finding symptomatic venereal disease, as has been demonstrated among Selective Service candidates and persons examined at the direction of courts or police. Contact investigation, the theoretically perfect method, has proved somewhat disappointing in practice, although the improvement demonstrated after conscious effort offers hope of better future performance.

It is important to note that contact investigation is the only case-finding device which, in theory, can reach all infectious cases. Education has its limitations because (a) it does not reach everyone, (b) presumably some venereal disease is symptomless in the early stages, and (c) individual persuasion is necessary to induce some persons to come for examination. Likewise, routine or mass serologic tests for screening purposes do not detect the presence of syphilis in the highly infectious seronegative primary stage nor in the stage before lesions develop, and in areas of low prevalence they are wasteful procedures. Contact investigation, therefore, remains the only universally applicable weapon which can function when all else fails and which will carry over into the era of controlled venereal disease. The disappointing result it has yielded heretofore, which is probably due to faulty technics, must not lead to its abandonment.

The need for wider participation of the private physician in case finding is evident. He is responsible not only for the administration of therapy, but also for the bringing of new cases to treatment. He should be greatly concerned with the education of the patient regarding the nature and the possible effects of the disease. Furthermore, either he or a trained health department

epidemiologist should obtain from the patient complete and accurate contact information, and the doctor's influence should be used in bringing exposed persons to examination.

All methods of case finding must be utilized to the utmost, the choice being determined by circumstances surrounding the individual situation. In addition, there must be a process of continuous improvement of old methods and development of new ones if the case-finding phase of the control program is to keep pace with the advance in therapeutic technics. —THE EDITORS

Analysis of Case-finding Methods in Community Venereal Disease Control

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United States Public Health Service

New methods of treatment of communicable diseases always direct attention to the possible necessity of varying the approach to the problem of control. The revolutionary changes recently introduced in the therapy of the venereal diseases have created a need for such a reevaluation in this field, particularly an increased emphasis on case finding. Unfortunately, many factors combine to render complete eradication of venereal diseases extremely difficult: the behavior pattern of the high incidence groups, failure on the part of the infected persons to recognize the disease, reluctance of some individuals to seek medical care for their infection, the incubation period of the diseases, the difficulties of diagnosis, the nonacceptance or ignoring of a valid diagnosis particularly when no signs or symptoms are noted, treatment resistance, and limitations in the criteria of cure. It is therefore important that, at all times, a venereal disease division keep a current record of its case-finding activities and that these be analyzed periodically to discover the most effective methods.

With this in mind, an analysis was made of the origin of cases admitted to the Norfolk City Venereal Disease Clinic for 1944. This group was chosen because it was available for study; but it should be pointed out that statistics on patients admitted to clinics do not give a complete picture, since they do not include individuals who consult private physicians. It may not be assumed that private patients would necessarily follow the same pattern. In fact, it is probable that, except for prenatal and premarital examinations, most of the cases in a private physician's practice are among patients who voluntarily seek medical aid.

Table 1 breaks down all admissions to the clinic by origin of case. As can be seen, Selective Service examinations were responsible for the greatest total number of cases, with voluntary admissions ranking second, and jail examinations third. Remarkably enough, contact tracing is fifth in bringing in total cases. In considering primary and secondary cases of syphilis, however, Selective Service examinations and voluntary admissions change place, the latter being responsible for three times as many as the former. Contact tracing is seventh in the number of admissions for primary and secondary syphilis.

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LE 1.—*Origin of all cases admitted to Norfolk City Venereal Disease Clinic in 1944*

Origin of case	Syphilis			Gonorrhea	Other venereal disease	Total
	Primary and secondary	Early latent	Late latent			
ive Service examination	23	425	509	84	13	1,054
tary	68	122	94	422	57	763
xaminations	14	39	18	445	..	516
red from other clinics	20	153	150	77	10	410
ict tracing	13	79	32	260	6	390
handlers' examinations	19	139	142	47	5	352
nissions	13	56	94	71	4	238
of one venereal disease mined for others	7	25	15	144	32	223
red from private physicians	15	22	19	17	1	74
arital examinations	3	26	28	11	3	71
	7	35	35	32	3	112
Total	202	1,121	1,136	1,610	134	4,203

LE 2.—*Comparison of number of cases of venereal disease admitted to the Norfolk Venereal Disease Clinic in 1944 through voluntary admission, epidemiology, and routine examination*

Origin of case	Syphilis			Gonorrhea	Other venereal disease	Total potentially infectious*	Total
	Primary and secondary	Early latent	Late latent				
emiologic	13	79	32	260	6	352	390
ine examination	66	654	712	731	53	1,451	2,216
ntary	68	122	94	422	57	612	763

ncludes primary, secondary, and early latent syphilis and gonorrhea

rther analysis of this table shows that origins of cases may be resolved hly into three groups representing dif- nt technics or case-finding devices: ntary application, epidemiology, and ine examination. Table 2 shows the lts that were obtained by these devices ie city of Norfolk in 1944.

ive times as many individuals with field positive lesions applied voluntar- for aid or were brought in through ine examination as were brought in active epidemiologic means. The last iod was likewise less productive of potentially infectious cases and total s than the other two. Routine exam- on uncovered more cases in the aggre- and more potentially infectious cases; ntary application, however, yielded ntly more cases of primary and sec- ary syphilis. All of this serves to t out the importance of community education, particularly concerning the availability of health services to the individual.

The following is a discussion of our experience in the use of these three methods. The discussion purposely avoids such factors as those of expense and the problem of personnel required as beyond the concept of this paper. It is felt that the methods which prove to be the most productive in case finding should be adopted and that the necessary arrangements should be made.

Beginning in June 1943 and rapidly expanding until September, a specially trained and diversified staff was assembled. This included 4 full time public health nurses, a medical social worker, 1 full time male investigator, 3 part time male investigators for evening work, and a pharmacist mate assigned by the Coast Guard. The Coast Guard uniform often aided in successful

field work.

The program emphasized epidemiologic case-finding methods with clinic time available morning, noon, and night. The field staff was directly under the supervision of the venereal disease control officer. Weekly conferences were held and modern medical and epidemiologic technics were discussed. In addition, short daily conferences were held by the field staff for general discussion and for the distribution and assignment of field work.

Each patient entering the clinic received a minimum of two interviews—one an interpretive interview and the second a contact interview. Patients were often given three or four interviews. Contacts were visited in the field on the day the information was received, and investigations were closed only when there appeared no possibility of finding the individual named. Arrangements were made with several military installations to furnish information by telephone, so that investigations were occasionally completed before the military contact form arrived.

However, in spite of all this, with a program literally built around epidemiology, and with an adequate staff under close supervision, epidemiology remained the least productive, by a large margin, of the three major methods of case finding. While careful questioning of the infec individual and prompt investigation of contacts named would theoretically app to be a slow but steady solution to venereal disease problem, in practical plication, even under the most ideal cumstances of adequate and trained p sonnel, the chain of infection can be f lowed for only one or two "links" and t becomes lost. Indeed, in a discouragin large number of cases, where no usable formation is obtained, no chain of inf tion can be traced. In addition, there main a number of individuals with kno infection or reasonable suspicion of inf tion who cannot be brought under c either because they are transients, or cause they refuse to accept treatment.

It will be noted (table 3) that fr civilian sources approximately 1 new c of syphilis or gonorrhea was discove for every 7 contacts named. (A la percentage are out of the local jurisdict or cannot be located because of inadequ information.) The same ratio of 1 tc prevails in reports on syphilis from m tary sources, but in reports concern gonorrhea the proportion is 1 new case 11 contacts named. These facts indic all too clearly how many of the kno foci of venereal disease cannot be reac by the epidemiologic approach.

TABLE 3.—*Number of named contacts brought to examination and found to be infec*

Results of investigations	Civilian contacts		Military contacts	
	Syphilis	Gonorrhea	Syphilis	Gonorrh
Total named	943	784	683	2,737
Number located	282	169	173	387
Percent of total located	29.9	21.5	25.3	14.1
umber infected	145	107	102	245
Percent of located infected	51.4	63.3	59.0	63.3

In addition, one faces also the factors of promiscuity and the incubation period of venereal diseases, both of which conspire to cause spread of the infection at a pace more rapid than can be coped with by the epidemiologic approach.

These considerations are not to be construed as depreciating the value of this approach or as recommending its discontinuance because of the time, effort and expense which it entails, but rather as p senting it in its proper perspective as adjunct to case finding rather than as solution to the problem of control. addition to the actual cases brought examination, one must realize that th are certain intangible benefits which acc from the epidemiologic approach. Inter is stimulated and patients are educated the control of venereal disease. This

cated by the fact that our workers have quently been questioned in the field con- ning clinic hours and examinations.

The second general case-finding method hat of routine examination. Unfortu- ly, except in highly selected groups, method is useful in uncovering syphilis , since the necessary examination for overing cases of gonorrhea cannot be e on a routine basis, particularly among ale patients.

The spreading of a serologic dragnet be achieved either by legal means or ough community education. However, use of coercive methods in a mass se- gic survey except under war emergency is likely to create an adverse public reaction. The arguments as to whether the ill effect on ultimate control of such a reaction outweighs any immediate benefits obtained in case finding are beyond the scope of this study.

At present, mass blood testing is largely confined to special groups. Table 4 gives the breakdown by such groups for patients admitted to the Norfolk clinic. Selective Service examinations, because of the numbers involved, uncovered more cases than any other group chosen for examination, in both the total number of cases and in the number of cases of primary and secondary syphilis.

BLE 4.—*Cases admitted to Norfolk City Venereal Disease Clinic in 1944 through routine examination*

Origin of case	Syphilis			Gonorrhea	Other venereal disease	Total
	Primary and secondary	Early latent	Late latent			
ctive Service examination	23	425	509	84	13	1,054
d handlers' examination	19	139	142	47	5	352
	14	39	18	445	0	516
es of one venereal disease amined for others	7	25	15	144	32	223
marital examination	3	26	28	11	3	71

Examinations for cards issued to the up of individuals who apply for food dlers' permits yielded the second highest nber of patients with darkfield positive ons found on routine examination. This s the sixth most productive of all the e-finding methods listed in table 1. In State such as Virginia with a relatively h incidence of venereal disease, the se- gic survey is an economical and easy e-finding device, although it is some- at discriminatory and the accidental nsmission of syphilis and gonorrhea are atively unimportant. This so-called food dlers' examination must, of course, be formed with the understanding that der no circumstances can the card be ized to certify the individual's freedom m venereal disease. The food handler mit simply should read that the indi- ual is permitted to handle food. Work- should be examined for those diseases ich can be transmitted by means of food, and a blood test is simply part of this routine check. In a State having a low incidence of disease this routine check may yield too small a return to make it practical, and other specialized selective procedures may have to be adopted.

In groups where a potentially high rate of infection might be expected, the effort expended on routine examinations is well rewarded by the discovery of new cases. Even in areas of low incidence the jail population constitutes such a group. From table 4, it can be seen that an examination of this group yielded the second highest total number of cases and the third highest number of cases of primary and secondary infection of any of the groups examined in routine fashion. When related to the number of persons involved, this "yield" becomes even more startling. In table 5 the results of examinations of persons arrested on sex charges or on charges of promiscuity are given. As many

as 67 percent of the white and 84 percent of the Negro offenders were found to be infected with a venereal disease; 63 percent of the white and 78 percent of the Negro patients were in infectious or potentially infectious stages. Combining a high degree of promiscuity with a high percentage of infectiousness, this group constitutes, for the purpose of control, one of the most important that can be examined.

TABLE 5.—*Percentage found infected with venereal disease among persons arrested on sex charges or on charges of promiscuity and examined at the city jail*

Result of examination	White	Negro
Not infected	33.4	16.2
Primary and secondary syphilis	1.3	5.4
Early latent syphilis	8.5	21.6
Late latent syphilis	3.5	2.7
Voluntary other than syphilis or gonorrhea	....	2.7
Gonorrhea	53.3	51.4
Total infected	66.6	8 38
Total examined	540	37

We must recognize that the basic maladjustment in many promiscuous individuals is often a psychiatric one and that venereal disease is only one of the consequences. Unfortunately, however, psychiatric rehabilitation to fit the individual into an acceptable social pattern is unsuccessful in the large majority of cases since apparently the maladjustment is deeply ingrained. Many of these individuals refuse to accept the diagnosis or to place themselves under treatment; they accept no responsibility for stopping the spread of the disease, and all too often pay no heed to interpretation and warnings concerning infectiousness. Bearing these things in mind, it is felt that the following provisions should be made: (1) that these individuals be subjected to most thorough and complete examination, (2) that they be forced to accept examination under the auspices of the health department so that complete examination may not be evaded by means of payment of bail or by obtaining an examination of a perfunctory nature, and (3) that they be confined and given intensive treatment for their infection.

The health department should be familiar with its legal authority and responsibi ity to force examination on individuals wl do not cooperate and who are potential or actually infectious. By judicious a infrequent use of the power of quarantir little antagonism will be aroused and de nite community benefit will ensue. If car ful explanation is made to those perso examined in jail that the health departme acts by order of the court and does n initiate jail confinement except under ra circumstances, it is probable that the will be little tendency to hide infectic While it is not within the province of t venereal disease division of the health d partment to cope with promiscuity as suc it is important that the health departme be vitally concerned with the definition promiscuity and its interpretation by t courts, and see to it that the judicia does not confuse venereal disease wi promiscuity.

Of the total number admitted, those w sought aid voluntarily comprised the gre est percentage of patients with prima and secondary syphilis. These individu are the antithesis of those who are exa ined under jail sentence. They are, for t most part, people who are interested enou in their own health to seek medical ca and to remain cooperative patients. Amo them, delinquency is a minor proble They accept diagnosis and hospitalizati and usually can be relied upon to refra from activities which may result in spre of the disease.

Because of the favorable showing patients who came in voluntarily, the No folk Venereal Disease Division conce trated its efforts during the past year methods by which more individuals co be induced to apply for aid. The hea education activities in Norfolk were rected through a citizens' committee venereal disease control. The commit clearly recognized that community inf mation was only the beginning in achievement of control. This work w divided among three subgroups as follow

1. Educational committee. Its functi was to furnish information to the public

2. Social protection committee. T group endeavored to secure such provisic

were necessary for adequate control in community, as improved jail facilities, ewomen, close liaison with the shore ol, vigorous measures against means of itation such as the misuse of taxicabs cabins.

Social hygiene committee. Long range ation is its objective.

other words, the first subgroup is to ly immediate publicity, the second is achieve the necessary facilities to with all the ramifications of the prob- and the third is gradually to improve community standards. In this paper, the activities of the first subgroup will liscussed.

s the problem was originally visualized, e seemed to be two groups of individ- in the community who need health ed- tion in venereal disease control: those directly need the services offered by health department and private physi- ns, and those who can help in getting ilities and personnel to make these serv- available. The first group includes ential patients; the second, citizens will- to recognize the community responsi- ty and to fight to achieve a complete trol program.

Because of the urgency of the problem ring wartime, health education in vene- l disease should stress the seriousness of se diseases and the availability of serv- s. Therefore, in publicizing the pro- m we were guided by the fact that a large proportion of the population s education need be only part of their eral knowledge, since they neither need aid of the program nor will they as- it unless they plan to participate. Such ups include civic clubs and various men's social, business, or garden clubs. e likewise realized that the broad social ects of the problem can be approached elligently only by long range instruc- n and planning.

The following means have been utilized educating the general public: news- ers, radio, billboards, trolley displays, ns, window displays, and posters.

Newspaper publicity was given to the nic, its hours and the services offered. tention was called also to the fact that private physicians are willing and anxious to treat the venereal diseases. In addition to feature articles, editorial backing was given. Large industrial concerns paid in full for newspaper advertising space covering five-eighths of a page and running in six editions in all the local newspapers including the one edited for the colored population. In addition, a series of twelve signed articles by different civilian and military personnel interested in various phases of venereal disease work was published. Some of the local industrial concerns carried a short slogan along with their regular advertisement, urging support of the venereal disease control program.

Evening radio round-table discussions were conducted at weekly intervals by members of the citizens' committee. In addition, transcriptions carrying the message in story form produced by the United States Public Health Service were played in the daytime. The use of spot announcements, however, was prohibited by the Office of War Information. Community education by means of the radio was continued over a 5-month period; the intensive newspaper publicity campaign ran for only 1 month.

Scattered in strategic areas throughout the city were twelve billboards carrying a venereal disease message. These were displayed over a 6-month period and were so well placed that it is probable that everyone in the city saw them.

For a period of 2 weeks, every trolley in the city of Norfolk carried a placard reading "Stamp Out Venereal Disease." A second intensive display was placed on every trolley 2 months later for another 2-week period, and, in addition, the displays were continued on about 10 percent of the trolleys for several months.

The films "Know for Sure" and "With These Weapons" were shown in all the Negro motion picture houses. Unfortunately, permission could not be obtained for showing these films in the theaters patronized by white people.

Four large windows in a department store on one of the busiest street corners in Norfolk were devoted to a display devised by the committee. Other commercial

concerns have agreed to allow the display to be shown in their windows, and it will be circulated in a number of strategic spots.

Posters were displayed throughout the city, in small store windows, in ferry and bus terminals, in taverns, in rest rooms, in industrial houses, and in drug stores.

In addition to general public education, talks were made to various social and business groups, including labor unions, civic clubs, the retail druggist association, the junior chamber of commerce, the United Service Organization and church groups. Because of the urgency of the problem, an attempt was made to limit these groups to those that could make specific contributions to the program. It was felt that much time and effort might be wasted unless some specific objective could be attained with each talk. For example, the junior chamber of commerce was addressed for the purpose of eliciting their interest in soliciting funds for the newspaper advertisement. The retail druggist association was approached for the purpose of obtaining a resolution supporting the display and distribution in drug stores of pamphlets concerning the control of venereal disease and condemning the sale of "remedies" for those infections over the counter. The labor unions were addressed in order to obtain their approval for industrial surveys and the distribution of pamphlets. The talk given to the boy scouts was for the purpose of obtaining their cooperation in distributing material. It is important that this utilitarian point of view be kept constantly in mind, for the inevitable question at the end of each talk is, "What can this organization do to aid?" It is at this point that the speaker should, if possible, have a particular project to offer. Of course, no community health program can ignore the groups which are of relatively little usefulness in facilitating the program, and many talks were given which simply fell into the category of general education. However, such talks are certainly of positive value in consolidating a favorable public opinion.

The importance of the private physician in a sound community health program is too well known to need further discussion. Certainly, it is essential that any such pr gram enlist his aid. With this in min letters were sent to each private physicia practicing in this community, and, in a dition, a visit was made by a public healt nurse to his office. The public healt nurse explained the function of the venere disease division of the city health depar ment, the purpose of the rapid treatme center, and the relation of the venereal di ease control effort to that of the priva physician. The reception was cordial every instance and these calls brougl about a closer understanding.

Coincidentally with this mass inform tion campaign directed toward the gener public and toward certain specific grou of the general public was begun the healt education program designed for the ind viduals potentially needing our service While it was recognized that some of t general education would filter down in the groups who needed service, it was al well known that many of these individua are almost completely untouched by new paper, radio, and other means of gener publicity. To reach this group, the fo lowing means were used: pamphlets, hon visits, payroll stuffers and proposals postemployment and preemployment blo testing.

Ninety thousand pamphlets were print for distribution in areas of a low econom level, presumably areas of high inciden of venereal disease. The printing was larg the language simple, and the message sho Each house in these areas received thr pamphlets at weekly intervals, each carr ing information on venereal disease a each presented in a slightly different ma ner. Clinic schedules were recorded.

These pamphlets were also distributed some of the cheaper hotels, where t turnover of guests is very rapid. Ho ever, resistance on the part of the manage who felt that the reputation of their esta lishments would suffer, limited the e fectiveness of this method. In fact, tho places in which pamphlets would have be of greatest value refused to permit the distribution.

Following agreement with the druggi association, the pamphlets were also plac

prominent display in 90 percent of the stores of the city and the owners ed to display posters and to dis- ute pamphlets to anyone requesting ven- l disease information or advice.

n effort was made to follow the dis- ution of pamphlets with home visits. r the third pamphlet had been dis- uted, homes were visited by a public th nurse. She encouraged individuals pply for tests and distributed appoint- t cards; or, in areas of known high lence, she attempted to obtain blood imens in the home.

fter a trial of several weeks of home ing, it was felt that the results ob- ed were not commensurate with the and effort expended in the homes. ng people, who presumably form the ntially infectious group, are not at e during the working hours of the pub- health nurse. The nurses found the distasteful. Home blood testing, how- , proved to be of definite value, par- larly if efforts were concentrated on ng individuals.

The citizens' committee wrote every cern in the community employing more n 15 persons, asking the manager or ier to permit a stuffer, devised by the erican Social Hygiene Association, to put into payroll envelopes. To date, with cooperation of the labor unions, 63 panies have agreed to distribute these ffers.

Whenever a company expressed willing- s to cooperate, a personal visit by the time male field investigator of health department followed. Postem- yment blood testing services were of- ed free of charge, to be done directly he industrial plant, and the larger com- ies were encouraged to introduce a sys- n of preemployment blood testing. The val Air Station and Naval Operating se, the Norfolk Navy Yard and several er companies have adopted this policy preeemployment blood testing, and 27 the 31 companies approached so far have eed to permit postemployment serologic veys. The acceptance of serologic sur- s in industry and union sanction for h a procedure are direct results of the community health education program. All blood testing is on a voluntary basis, and when a positive serologic test for syphilis is discovered, the individual is referred to a private physician or to the clinic, without the knowledge of the employer.

In an attempt to analyze the relative merits of the various health educational approaches used, each patient who applied voluntarily to the clinic during the 3-month period of October, November, and December, 1944, was asked if he was influenced by the publicity. However, it was soon discovered that many individuals were reticent about admitting the true reason for their application and frequently gave the convenient excuse of wanting a health card. Some of these persons admitted, on reinterview, that reading the billboard or pamphlet prompted them to come.

A better method of analysis is to compare the origin of cases admitted during October, November, and December, 1943, and that of those admitted during the same months in 1944. Insofar as can be determined, the two 3-month periods are comparable from the standpoint of clinic efficiency, epidemiologic staff and general clinic management, and consequently form a fair basis for measuring the results attributable to the community health program adopted in the latter period.

Chart 1 shows the origins of all cases admitted during the two periods. It will

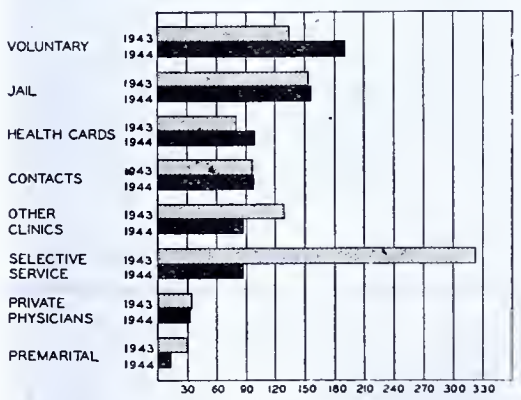

Chart 1.—Total number of cases admitted to the Norfolk City Venereal Disease Clinic during October, November, and December, 1943–1944.

be noted that the two origins which brought in appreciably more cases during the latter period are voluntary admissions and examinations for health cards. Certainly the increase in voluntary admissions may be attributed almost wholly to increased knowledge on the part of the public resulting from the community health program, and it is probable that the examinations for health cards may be in part a reflection of that work. That this increase was entirely confined to infectious and potentially infectious cases can readily be seen from chart 2. The only group of voluntary admissions that showed no increase was that of late latent syphilis.[2]

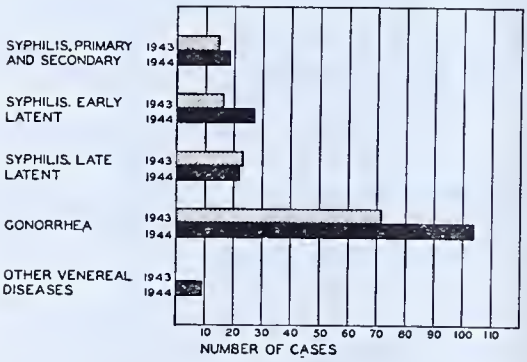

Chart 2.—Number of cases voluntarily seeking treatment at the Norfolk City Venereal Disease Clinic during October, November, and December, 1943 and 1944.

It may be worth noting that in regard to epidemiologic effort there was a slight improvement, in that 59 percent of cas with usable information were broug under treatment in 1944 as compared wi 51 percent in 1943. It is also noteworth that there was no perceptible change the number of jail examinations, for t total number of examinations and cas found were practically identical for the tw periods.

A comparison of the total number blood tests taken in these periods may al be of interest. Exclusive of Selective Se vice examinations, a total of 15,130 ser logic tests for syphilis was performed Norfolk in the last 3 months of 1944, contrasted with 10,522 in the last 3 mont of 1943. This increase is a definite indi tion of heightened public interest.

Effects of the program are likewise a parent in a comparison of the number patients going to the rapid treatment c ter during the 3 months preceding t program with the number attending d ing the 3 months of the program. W the opening of the community educatio program, there was a decided increase the number of patients willing to go the Hampton Roads Medical Center, ev though approximately the same amount effort was expended in this direction by clinic staff. Undoubtedly, some of t increase was due to patient-to-patient ucation, one of the most satisfactory ty of community education in the long r but some of it was also undoubtedly c directly or indirectly to the health edu tion program.

As of the present report, the hea education program is not quite compl but the trends of its results are clear. T city has been saturated with informat concerning availability of treatment venereal disease by private physicians a

[2]That the trend toward increased voluntary admission of potentially infectious cases is continuing is indicated by the fact that there were 434 voluntary admissions from January through April, 1945, compared with 189 in a similar period of 1944. The percentage of potentially infectious cases among these voluntary admissions was 87.3 in 1944 and 82.1 in 1945.

TABLE 6.—*Admissions to Hampton Roads Medical Center July–December 1944*

Type of case	July	August	September	October	November	Decer
Primary and secondary syphilis	17	7	12	34	17	16
Early latent syphilis	10	6	4	9	21	25
Late latent syphilis	2	4	..	4	6	3
Gonorrhea	38	31	32	67	73	48
Other venereal diseases	1	1	1	1	5	2
Total	68	49	49	115	122	94

ie clinic. With continued, though perıps less intensive, education of this type, is felt and hoped that if and when the eed arises, individuals will recall the vailability of services and will utilize ıem. On the other hand, it is important) recognize that health education is only reliminary to a complete control program. Ve must realize that even the most comlete saturation of the community with inɔrmation will at best result in only partial ontrol, for this approach appeals only to ıose individuals sufficiently interested in heir health to do something about it. ;tress must be placed upon the fact that ıany in the high promiscuity group canıot be reached by an approach through ommunity education. There is also a ;roup who to prevent detection will atempt self-medication. Hence, community nformation can be only the beginning of a vell rounded control effort.

A complete community program is yet o be achieved in Norfolk, since the city s still lacking in facilities and personnel to leal adequately with promiscuity and facilitation. Without such community support, the health department must continue to function on the periphery of an ever increasing residue of venereal disease.

CONCLUSIONS

1. New methods of treatment of the venereal diseases direct the efforts at control primarily toward case finding.

2. Even the most vigorous "from whom to whom" approach to the problem can only be an adjunct to other case-finding methods. It is probable that the venereal disease field staff of the future will be a smaller but a more highly specialized group whose efforts will be almost completely devoted to case finding and community education.

3. Mass blood testing if done on a large enough scale in an area of high incidence will uncover more cases of syphilis than any other method employed.

4. The greater the potential incidence in a given group (e.g., jail population), the more thorough should be the examination, particularly in the case of gonorrhea.

5. In Norfolk, more individuals with infectious lesions voluntarily applied for aid than were brought under care by any other means. Because of this, community education should constantly stress availability of services.

6. Intensive community education in venereal disease should be directed primarily toward two types of individuals: (a) Those who need venereal disease service, (potential patients), and (b) those who can help in making those services available and can aid in obtaining the necessary facilities and personnel.

7. Intensive education is of distinct value in publicizing the availability of community venereal disease service and in stimulating individuals sufficiently interested in their health to apply for venereal disease examination.

8. Community education is of little benefit in reaching certain individuals whose attitude is such that they accept neither diagnosis nor responsibility for the prevention of the spread of these diseases.

9. Health education, even when applied in intensive fashion, is not to be regarded as a complete solution to the problem of venereal disease control, but rather as the preliminary step toward achieving an aroused public willing to deal with all the necessary ramifications of the problem, including long range objectives.

10. Intensive community education to be successful must be directed toward case finding and toward the groups of high incidence and must be restricted to immediate objectives. The broad aims can be achieved only by an integration of social hygiene concepts with long range public education and community participation.

Syphilis Control Through Mass Blood Testing

W. H. Y. Smith, M.D., C.P.H.,[1] Lida J. Usilton, M.A.,[2] and Martha C. Bruyere[3]

The compulsory Selective Service registration, effective Oct. 16, 1940, of all men between the ages of 18 and 40, inclusive, offered a splendid opportunity for mass blood testing. Several areas, including Alabama, took advantage of the opportunity and set up machinery whereby any registrant who desired might be given a blood test free of charge. Corps of workers were assigned to draw blood in different groups of counties in Alabama on different dates, so that the whole State was covered within 6 weeks following registration. The reading of the tests in the State laboratory was completed by the end of another 5 months. As positive blood tests were encountered, those persons suspected of having syphilis were notified by letter, with instructions to seek treatment.[4]

Approximately 200,000 registrants, constituting some 60 percent of the total, availed themselves of the offered service. Negro registrants responded more readily than did white registrants, so that proportionally many more Negro than white men were tested. Tests were successfully completed on 113,363 white and 80,675 Negro registrants. Of these, 1,999 and 17,652, respectively, gave positive results. Presumably the majority of these represent newly discovered cases, since individuals who already knew of their infection would not be apt to volunteer for testing.

Detecting syphilis, however, does little good if the individuals found to have positive serologic reactions are not brought to examination and to treatment. It is the purpose of this discussion to examine the record of admissions to the public clinics in Alabama in order to determine the number of these cases that were brought to treatment as a result of the free testing offered registrants.

The services of a mechanical tabulating unit have been available to the syphilis clinics of Alabama since early in 1940 and a satisfactory record is thus at hand. The two accompanying charts trace this

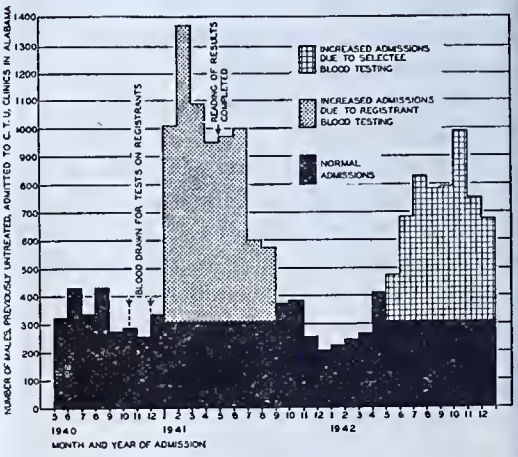

Chart 1.—Male admissions for **untreated** syphilis to central tabulating unit clinics in Alabama from May 1940 through December 1942.

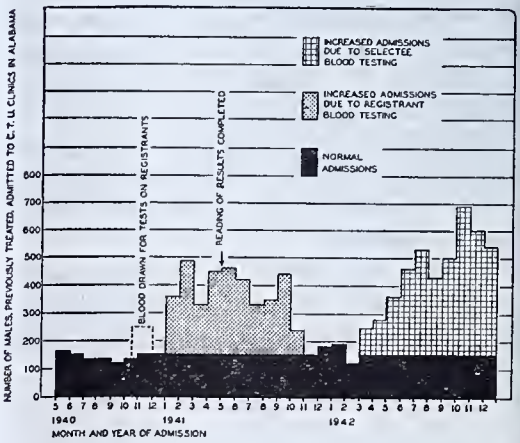

Chart 2.—Male admissions for **treated** syphilis to central tabulating unit clinics in Alabama from May 1940 through December 1942.

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[1]Director of Division of Venereal Disease Control, Alabama State Department of Public Health, Montgomery, Ala.

[2]Principal Statistician, Venereal Disease Division, U. S. Public Health Service.

[3]Statistician, Venereal Disease Division, U. S. Public Health Service.

[4]The results were tabulated and published (*1*). A description of the methods and a summary of the results appeared in Venereal Disease Information, January 1943 (*2*). Dr. A. J. Perley evaluated the results and follow-up activities carried on in Chambers County (*3*).

ord from May 1940 through December 2. Chart 1 covers male admissions of v untreated cases, while chart 2 traces admissions of male patients who had eived previous treatment for syphilis. t will be observed that no marked nges in admissions to Alabama clinics k place until January 1941, about 1 nth after the securing of specimens m registrant volunteers had been com-ted. At this time. the admission rates reased severalfold. The increase in clinic nissions occurred in two waves. The st may be associated directly with the luntary testing program, while the sec-d undoubtedly reflects the cumulative luence of the compulsory serologic tests de in connection with the induction ex-inations.

ADMISSIONS OF NEW CASES

The monthly average number of pre-usly untreated male patients admitted central tabulating unit clinics in abama for the last 8 months of 1940 s 330. The highest number admitted in y one of these months was 431 (in gust). Altogether there were 2,638 new le admissions between May and Decem-r 1940, inclusive. In January 1941 ad-ssions jumped to more than 1,000, and February they reached a high of nearly 400. The higher admission rates were aintained through June of that year (2 nths after the last blood was read), and d not drop below the highest number mitted in any one month in 1940 until ptember 1941. During 8 months, January rough August 1941, 7,556 male patients t previously treated for their infection ere admitted to syphilis clinics in Alabama, increase of 4,918 cases over the preced-g 8 months. The admission rate had been irly constant in 1940, and it returned to proximately the same level after August 941. It seems fair then to assume that, r the most part, the difference between e number of male patients admitted dur-g the last 8 months of 1940 and the mber admitted during the first 8 months 1941 represents the number of positive gistrants that were brought to treatment s a direct result of the blood tests.

Approximately 5,000 new cases over and above those who would have normally been admitted to clinics were brought to treatment following the voluntary free blood testing of registrants. Presumably a similar increase occurred in patients treated in private practice. The magnitude of this latter group may be roughly approximated by means of the percentage of admissions to different types of treatment sources obtained from the survey made of the State of Alabama during 1940 (*4*). For the age group comparable to the section of the population required to register, it was found that 6 percent of the male clinic admission were white and that they represented 49 percent of all white male patients seeking treatment, while the 94 percent of the male clinic admissions that were Negro constituted 89 percent of all male Negroes seeking treatment. On this basis it is estimated that, of the 4,918 male persons with positive serologic findings who came to treatment in clinics as a result of the blood tests, 295 were white and 4,623 were Negro, and that, in addition, 305 white men and 571 Negroes sought treatment outside public clinics. This yields the following approximation to the total increase in new untreated admissions: 600 white men and 5,200 Negro men, a total of 5,800, nearly 30 percent of all the positive serologic reactions found.

READMISSIONS

From chart 2 it can be seen that there was also a rise in the admission rate of previously treated syphilitic patients. From May through December 1940, the average monthly number of male patients admitted to central tabulating unit clinics, who had previously received antisyphilitic treatment, was 139, while the highest number for any 1 month in the period was 164. In January 1941 admissions rose to 357, and in each of the subsequent months through October 1941 they exceeded the highest month's admissions for 1940. Admissions dropped to 146 in November 1941 and remained at the 1940 level for several months, until Selective Service blood testing caused another increase in admissions during 1942.

Admissions in the 10 months, May through December 1940 and November and December 1941, totaled 1,442 cases, whereas during the first 10 months of 1941, they totaled 3,862. As in the case of new admissions, the difference of 2,420 may be attributed to the registrant testing with its attendant publicity. An allowance for patients seeking treatment from private physicians raises this estimate to 2,852, 296 white and 2,556 Negro.

ALL ADMISSIONS

Combining the estimated excess of admissions of new cases with the estimated excess of readmissions, we find that in the period following the voluntary free blood testing approximately 8,650 persons with positive blood tests sought treatment for syphilis; this was in addition to the normal admissions. Not all of the increase in admissions can be taken to be the direct result of the voluntary blood-testing program carried out among registrants. Compulsory blood testing under Selective Service, which began soon after registration, undoubtedly accounted for some of the increase.

While it is impossible to make a precise allocation of the increase as between the influence of the voluntary and that of the compulsory blood testing, there is reason to believe that the effect of compulsory testing on clinic admissions in the first 8 to 10 months of 1941 was comparatively small. A rough estimate may be made. From its inception in the fall of 1940 to September 1941, the Selective Service System found about 3,500 registrants with positive blood reactions in the State of Alabama.[5] Since 60 percent of all the registrants had been tested voluntarily within 6 weeks after registration, allowing for the fact that known syphilitics are less apt to volunteer for testing, it may be assumed that about 2,350 of the 3,500 had not taken the voluntary blood test. Some of these must have already been under treatment at the time of the examination. But even if we assume that all of these were newly discovered cases and that they applied for treatment in the same proportion as those detected by the voluntary testing program, the total admissions resulting from the compulsory examinations would be about 900.[6] This would leave approximately 7,800 cases of syphilis which were brought to treatment for the first time or were returned to treatment, as a result of the voluntary mass free blood-testing program. This constitutes 40 percent of the number discovered or about 25 percent of all the estimated number of syphilitic individuals in the group included in the program.

SUMMARY

1. At the time of compulsory Selective Service registration, Alabama offered all registrants free blood tests.

2. Tests were successfully completed on 113,363 white and 80,675 Negro registrants, of whom 1,999 and 17,652, respectively, gave positive serologic reactions.

3. The admissions to public clinics in Alabama made available through the central tabulating unit reports were studied for the period from May 1940 through December 1942 in an effort to determine the efficacy of such a blood-testing program in bringing cases to treatment.

4. A marked increase in admissions to Alabama clinics took place in January 1941, about 1 month after the last registrant had reported for his blood test. The admission rates increased severalfold before all the blood specimens had been examined.

5. During the months immediately following voluntary free blood testing, approximately 5,800 new untreated cases

[5] Based on the serologic reports for the first two million examined (*5*). Only 3,300 positive slips were received up to Sept. 1, 1941, from the State of Alabama. This figure is raised to 3,500 in order to account for the lag between examinations and receipt of blood slip.

[6] The number of cases per thousand selectees tested was consistently higher than the number per thousand registrants, for the age and race groups for which comparable data were available. From the difference in these rates, it was estimated that about 27 percent more of the known syphilitic group failed to volunteer for testing than of the general population. This estimate was used in computing the approximate number of the 3,500 selectees found to have positive serologic reactions, who came to treatment through selectee rather than registrant blood testing.

bove the normal admission were brought
› treatment. These constituted 30 percent
f the 19,651 cases uncovered by the tests.

6. There was a corresponding rise of ,850 cases in the admissions of previously reated cases of syphilis.

7. Even taking into account the con-omitant Selective Service compulsory lood testing, a mass voluntary free blood-esting program was responsible for ap-roximately 7,800 admissions for syphilis to arious treatment sources in Alabama eyond the normally expected number. hese admissions constituted 40 percent of he cases uncovered by the program, or 5 percent of the estimated cases existing n the population under study.

8. A similar increase in admissions, hough smaller in magnitude, followed the ntensified Selective Service blood testing n 1942.

CONCLUSION

We may conclude from the experience in Alabama that mass blood testing carried on among a population containing a large proportion of Negroes and also having a relatively high syphilis rate is an effective tool both in uncovering the existing syphilis in the population and in bringing potentially infectious cases under treatment.

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Contact Investigation as a Case-finding Instrument

There are three principal methods of venereal disease case finding: education, screening tests, and contact investigation. Education in its broader sense includes among other types the community education which induces people to go to a physician or clinic when they "suspect" venereal disease. In order for such suspicion to be aroused by the appearance of symptoms, the patient must have some knowledge of venereal diseases and how they are acquired. An educational program would also influence people without symptoms to seek diagnosis because of a desire to make certain venereal infection was not present. Such desire is created by posters, films, educational lectures, and pamphlets.

Table 1 shows the contribution of the various case-finding methods to the number of new admissions in approximately 180 clinics serviced by a Public Health Service regional tabulating unit. It is seen that approximately half of the admissions with primary and secondary syphilis come to treatment voluntarily. These are the persons who come to treatment because of the presence of symptoms or of the suspicion of infection. Only 20 percent of the early latent cases come for this reason, which is to be expected because of the absence of symptoms. Approximately 36 percent of

Based on data contained in semiannual and monthly reports furnished by regional tabulating units through the courtesy and cooperation of the following State and city officials: Dr. G. F. Manning, Superintendent of Health, Arizona; Dr. Wilton L. Halverson, Director of Public Health, California; Dr. Henry Hanson, State Health Officer, Florida; Dr. Grady F. Mathews, State Health Commissioner, Oklahoma; Dr. Harold M. Erickson, State Health Officer, Oregon; Dr. Benjamin F. Wyman, State Health Officer, South Carolina; Dr. Herman N. Bundesen, President, Chicago Board of Health, Chicago, Ill.; Dr. Theodore Rosenthal, Director, Bureau of Social Hygiene, New York, N. Y.; Dr. J. F. Bredeck, City Health Officer, St. Louis, Mo.; Dr. George C. Ruhland, Health Officer, Washington, D C.

Prepared in the Statistical Section, Venereal Disease Division, U. S. Public Health Service, by Albert P. Iskrant, M. A., Sanitarian (R).

the gonorrhea patients and 49 percent of those with other venereal diseases were voluntary applicants for treatment.

In primary and secondary syphilis, a higher percentage of males than females come to treatment voluntarily: (46.8 vs. 42.8). The same is true in gonorrhea (57.5 vs. 24.7), and in other venereal diseases (56.1 vs. 40.2). On the other hand, in early latent syphilis, a higher percentage of females than males come to treatment voluntarily (23.8 vs. 12.1). The only significant race differential is the consistently higher percentage of Negro females than white females who come to treatment of their own accord (29.9 vs. 17.8) and except in primary and secondary syphilis, a higher proportion of white males than Negro males (61.3 vs. 42.5).

Another type of education which may be quite profitable in case finding is education of the individual patient. It may be utilized in two ways: as a method of getting patients to return for treatment if again infected, and as a method of inducing patients to bring friends to the clinic for examination or treatment. This is related to the contact investigation process, as sometimes patients may be induced to "bring their friends in" even though not admitting these friends are sexual contacts.

Screening tests attain their chief value in an area of high prevalence or among a group with a potentially high prevalence. Naturally, the higher the prevalence rate the greater the number of cases found. This is demonstrated by the volume of new admissions among persons referred to the clinic by law enforcement authorities. According to table 1, 7 percent of the primary and secondary syphilis cases, 8 percent of the early latent syphilis cases, 24 percent of the gonorrhea cases, and 12 percent of the other venereal diseases were found by examination of law violators. The proportions of females were higher, being 20.8 for primary and secondary syphilis; 32.2 for early latent syphilis; 52.7 for gonorrhea, and 33.3 for other venereal diseases.

Selective Service blood testing has been a very profitable case-finding instrument. Seven percent of the primary and secondary syphilis cases, 21 percent of the early latent, 3 percent of the gonorrhea, and 8 percent of the other venereal diseases admitted were discovered by such examinations. It should be borne in mind, however, that due to the decrease in volume in 1944, Selective Service examinations were losing their effectiveness as a venereal disease case-finding instrument. Table 2 shows a considerable decline in the yield from this source in the last half of 1944 as compared to the first half of 1944.

It is noteworthy that a routine testing program such as that of the Selective Service can be so fruitful in uncovering cases with open lesions of syphilis. During the first half of 1944, in one State, Selective Service contributed 23.2 percent of the primary and secondary admissions to clinics, while in another State, it contributed only 0.9 percent. The number of open lesions discovered is a function of the physical examination—a complete examination will reveal open lesions; a perfunctory drawing of blood will not. As shown in table 1 other such routine testing as industrial, premarital, prenatal, and food handlers' examinations uncovered 14 percent of the primary and secondary syphilis cases, 30 percent of the early latent syphilis, 10 percent of the gonorrhea, and 9 percent of the other venereal diseases.

As the prevalence of a disease decreases, routine or screen testing tends to lose its value as a means of case finding. Obviously in an area of high prevalence the yield in terms of new cases will be high, but in an area of low prevalence the cost of finding cases through screen testing becomes prohibitive. Contact investigation is an instrument which can be used at any time in any area for finding infectious venereal disease. Theoretically, it offers the perfect tool for breaking specific chains of infection and for this purpose should be equally effective and economical regardless of the prevalence of the disease. Its advantage over other methods is that it brings about the examination of persons at the time they are potentially infectious. These persons may not respond to education because of the absence of symptoms, the failure to recognize symptoms, or the reluctance to present themselves for ex-

ination. Routine testing cannot detect e presence of the disease in the prelesion open-lesion seronegative stage and, reover, cannot be performed with sufient frequency to detect a large proporn of infectious cases. It is an epidemiogic principle that for each new case of nereal disease discovered there exists in community at least one other case of ectious venereal disease. If the disease ntinues to spread, there must be more an "one for one." Therefore, through rfect contact investigation it should be ssible to discover at least one infected rson (the source) for each case reported for treatment. In addition, it should possible to locate all persons to whom e patient may have transmitted the inction.

The figures in table 1 indicate that only percent of the primary and secondary philis, 11.0 percent of the early latent, .1 percent of the gonorrhea, and 8.7 percent of the other venereal disease cases me to treatment because of contact investigation. However, it should be borne mind that this item, "reason for admison," was probably checked by the clinic erk who may not have known, in many stances, the real reason for coming to eatment. An analysis of the results of ntact investigation permits determination the results of this method of case ding.

In table 2 are included all cases brought treatment in clinics as a result of contact investigation, calculated as a percentge of all new admissions to clinics. Contacts of the Armed Forces produced 3.1 rcent of the primary and secondary lmissions to clinics from January through ne 1944, 1.9 percent of the early latent philis, and 11.6 percent of the gonorrhea. rom July through December 1944, the rcentage of primary and secondary philis had dropped to 2.4, early latent 1.0, and the gonorrhea percentage to 9.5. is noteworthy that the contribution of ntacts of the Armed Forces to the volne of case finding is greater in gonorrhea an in syphilis. In the first 6 months of 944, the contribution of civilian contact porting to clinic admission for primary and secondary syphilis was 10.5 percent, early latent 9.2 percent, and gonorrhea 8.5 percent. In the last 6 months of 1944, these proportions had increased to 12.0, 10.1 and 13.2 percent, respectively. The increase is encouraging and is in line with other data concerning contact investigation. The most disappointing aspect of contact investigation is in the low yield of primary and secondary syphilis. Since all admissions with primary and secondary syphilis offer opportunities to seek out source and spread contacts, why does not the process lead to discovery of these cases?

In an attempt to analyze the contact investigation process, table 3 has been prepared. It shows the ratio of contacts reported per new case of primary and secondary syphilis, the number infected and under treatment, and the "epidemiologic index." The index is the ratio of infected contacts to the original admissions reporting contacts. It includes cases brought to treatment as a result of the contact investigation as well as cases under treatment prior to investigation. The minimum index should be "1" and as the disease is believed to be spreading, at the present time it should be greater than 1. (How much greater we do not know.) It is seen that for a group of 5 States for which data are available, the index was 0.25 in the period from July through December 1943; 0.38 in the period from January through June 1944, and 0.42 from July through December 1944. The increase is encouraging and offers some hope that contact investigation can be improved. As Heller pointed out in his address to the 1944 National Conference on Venereal Disease Control[1], "the contact investigation process is not an easy one"—and the fact that consistent improvement has been shown in the past 18 months offers hope that still greater improvement may be made. Another observation which offers much encouragement is the fact that the "index" is not universally low but varies from a low of 0.15 in one State to a high of 0.55 in another in the period from July through December 1944. For

[1]Heller, J. R., Jr.: Venereal disease control of tomorrow. J. Social Hyg., 31: 16–25, 1945.

some clinics in these States the index calculated has been greater than "1." One item not included in this figure deserves special comment—the cases of one venereal disease discovered in persons reported as contacts to persons infected with another venereal disease. Table 4 shows the number of cases of venereal disease (other than the disease of the informant) found among contacts examined. It is seen that of the syphilis contacts, 4 percent were infected with gonorrhea, and of the gonorrhea contacts, 4 percent were infected with syphilis. Among contacts of other venereal diseases examined, 4.5 percent were infected with syphilis, and 9.7 percent with gonorrhea. These are probably minimum figures. A person suspected of any venereal disease should be examined for all venereal diseases.

In table 3, data are also shown concerning the number of cases of syphilis with open lesions brought to treatment as a result of investigation of contacts of patients with primary and secondary syphilis. It is seen that for every 100 cases of primary and secondary syphilis admitted to clinics only 8 additional cases were newly discovered through contact investigation, or 0.08 for one.[2] The highest figure attained in any area from which data are available is 0.14. Of course, many of the cases brought to treatment in the presumably latent stages may, in fact, have been discovered and treated before secondary lesions would ordinarily have appeared. Nevertheless, this is perhaps the most discouraging aspect of the contact investigation process. Why cannot more than 8 to 14 cases of primary and secondary syphilis be found by investigation of the contacts of 100 primary and secondary syphilis cases?

The volume of contact reporting is one factor and possibly the most important. The ratio of contacts reported per new case has increased from 0.95 during the last half of 1943, to 1.27 the first half of 1944, to 1.52 in the last half of 1944. The improvement is encouraging, but since family contacts are included in this ratio it is still very low. The epidemiologic index is a function of the volume of contacts reported. Evidently the volume of contact reporting must increase.

Not only must there be volume in contacts reported but sufficient information must be provided so that named contacts can be located. Of the nonfamilial contacts of early syphilis reported in 9 States in the period from July through December 1944, a complete name and address was reported in only 55 percent. In the same period only 36 percent of the cases in which a complete name and address was lacking was examined, compared to 62 percent of those in which a complete name and address was reported. Obviously the extent and accuracy of information on contact reports must be improved.

The recording of complete information on the contact report in itself does not bring cases to treatment. Contacts must be induced by letter or visit to come to the clinic or to a private physician for examination. This is probably one of the best developed technics in the contact investigation process. The percentage examined of those for whom a complete name and address was reported has improved from 56 percent in the period from July through December 1943, to 62 percent in the period from July through December 1944. In some areas, the percentage examined within 60 days is as high as 75. This means that in States in which efficient investigators are employed, health departments are able to bring to examination within 60 days approximately 3 out of 4 contacts for whom a complete name and address is reported. Variation of efficiency in the investigative process is indicated by the fact that this percentage falls as low as 32 percent in some areas. Among contacts for whom incomplete information was reported, the percentage examined ranged from a high of 62 to a low of 10. O

[2]An explanation should be offered regarding the variation in the figure 12 percent in table 2 and the figure 0.08 in table 3 regarding primary and secondary syphilis. The 12 percent figure represents the contribution of the investigation of contacts reported by all civilian patients, the 0.08 (or 8 per 100) figure represents the "yield" of investigation of contacts of patients in these same clinics.

the group reported in table 3, out of every 100 patients with primary and secondary syphilis only 87 contacts were examined and 42 were found to be infected.

In these areas, therefore, in order to obtain an epidemiologic index of 1 and with the same level of investigation and completeness of information it would be necessary to increase the volume of contact reporting approximately 2½ times, to a ratio of 3.8 per patient. An improvement in the type of information or an improvement in the investigative process would further improve the index. Although the attainment of an index of 1 may not bring about the complete eradication of syphilis it would at least be the achievement of a minimum goal. It is realized that locating and treating infectious cases is more important than the attainment of any mathematical index. Reduction of the incidence of the disease is the important objective; the index is only a mathematical indication of the degree of attainment of this objective.

In order to break chains of infection, cases should be located and brought to treatment in the infectious stages and before the infection has been spread. And although locating the source of infection is undoubtedly important, too much emphasis has been placed upon it, especially in syphilis, and too little upon locating the "spread" contacts. All too often the "sources" have passed into the latent stage before they are located and examined. The persons to whom the patient may have given the disease are more likely to be in the open-lesion or prelesion stage when examined and to offer one of the best opportunities for the prevention of further spread of infection. Interviewers, therefore, should attempt to obtain the names of all exposures within a reasonable period and not seek merely to determine the "source," which cannot always be specifically identified.

SUMMARY

1. According to 1944 data on recorded "reason for admission to clinic" more patients with symptomatic venereal disease come to treatment of their "own accord" than for any other reason.

2. The various types of "routine" testing, including Selective Service testing, contributed heavily to the volume of admissions but were responsible for a proportionately higher percentage of admissions of early latent syphilis than cases of symptomatic venereal disease.

3. In the period from July through December 1944, in 5 States for which data are available, contact investigation contributed 14.4 percent of the primary and secondary syphilis admissions, 11.1 percent of the early latent syphilis, and 22.7 percent of the gonorrhea admissions.

4. Consistent improvement has been shown in contact investigation in these areas throughout 1943 and 1944, resulting in an increase in the "epidemiologic index" for primary and secondary syphilis from 25 in the last 6 months of 1943 to 38 in the first 6 months of 1944, and to 42 in the last 6 months of 1944.

5. This has been accomplished by a consistent improvement in the volume of contact reporting, resulting in an increase in the ratio of contacts reported per new admission with primary and secondary syphilis from 0.95 in the last 6 months of 1943 to 1.27 in the first 6 months of 1944, and to 1.52 in the last 6 months of 1944.

6. This improvement was accompanied by an increase in the percentage examined among contacts reported. During the last 6 months of 1944, 62 percent of contacts reported with a name and address was examined, compared to 56 percent in the corresponding period of 1943. Some areas are now examining within 60 days more than 75 percent of the contacts for whom a name and address is reported and more than 50 percent of the contacts with incomplete information.

7. Along with continued improvement in the factors enumerated two additional aspects of contact reporting should be emphasized. More attention must be paid to the so-called "spread" contact, and machinery must be established to obtain contact information from private physicians and institutions so that contact investigation may enter and attempt to break all "chains of infection."

TABLE 1.—*Reason for admission to treatment during 1944 as checked on morbidity reports of clinics in a group of States serviced by a regional tabulating unit*

Reason	Primary and secondary		Early latent		Gonorrhea		Other venereal disease		Total	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Of own accord	661	44.5	907	19.8	3,913	35.6	495	49.3	5,976	33.1
Referred by private physician	122	8.2	234	5.1	306	2.8	47	4.7	709	3.9
Contact investigation	102	6.9	501	11.0	1,876	17.1	87	8.7	2,566	14.2
Selective Service examination	101	6.8	949	20.7	312	2.8	84	8.4	1,466	8.1
Law violation or jail examination	108	7.3	363	7.9	2,631	24.0	125	12.4	3,227	17.9
Routine	207	13.9	1,360	29.7	1,141	10.4	90	9.0	2,798	15.5
Referred by another patient	2	0.1	24	0.5	19	0.2	1	0.1	46	0.2
Other	183	12.3	240	5.3	780	7.1	74	7.4	1,277	7.1
Total	1,486	100.0	4,578	100.0	10,978	100.0	1,003	100.0	18,045	100.0

TABLE 2.—*Contribution of various case-finding methods to volume of admissions to clinics during 1944*

Period	Contacts of Armed Forces		Contacts of civilians		Selectees		Clinic admissions	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Primary and secondary syphilis:								
Jan.-June, 1944	35	3.1	118	10.5	146	13.0	1,125	100.0
July-Dec., 1944	28	2.4	138	12.0	21	1.8	1,151	100.0
Early latent syphilis:								
Jan.-June, 1944	65	1.9	315	9.2	974	28.6	3,410	100.0
July-Dec., 1944	25	1.0	252	10.1	174	7.0	2,487	100.0
Gonorrhea:								
Jan.-June, 1944	809	11.6	588	8.5	84	1.2	6,953	100.0
July-Dec., 1944	826	9.5	1,151	13.2	24	0.3	8,717	100.0

TABLE 3.—*Results of investigation on contacts of clinic* patients admitted with untreated primary or secondary syphilis*

Period	Clinic admissions (previously untreated)	Contacts reported	Contacts reported per clinic admission	Contacts found infected			Epidemiologic index	Contacts brought to treatment with lesions	Contacts brought to treatment with lesions per clinic admission
				Brought to treatment	Under treatment prior to investigation	Total			
July–Dec., 1943	1,541	1,458	0.95	182	197	379	0.25	(**)	(**)
Jan.–June, 1944	1,598	2,024	1.27	269	335	604	0.38	98	0.06
July–Dec., 1944	1,626	2,479	1.52	268	408	676	0.42	125	0.08

* Clinics in 5 States serviced by regional tabulating units.
** Data not available this period.

TABLE 4.—*Cases of venereal disease, other than that of the informant, discovered among examined contacts of venereal disease patients*

Disease of informant	Number examined	Syphilis found		Gonorrhea found		Other venerea disease found	
		Number	Percent	Number	Percent	Number	Percent
Syphilis	2,728	.....	.....	107	3.9	2	0.1
Gonorrhea	4,853	183	3.8	.....	.....	9	0.2
Other venereal disease	309	14	4.5	30	9.7	.....	.....

DIAGNOSIS

Interpretation of findings in the cerebrospinal fluid. Carl Lange and Albert H. Harris. Arch. Neurol. & Psychiat., Chicago, **53**: 116–124, Feb. 1945.

The authors define the term, "dementia paralytica formula," state the 5 obligatory tests for the diagnosis of dementia paralytica, discuss the qualitative and the quantitative aspects of the formula, and report 4 cases of the disease in the early or asymptomatic stages.

The term, "dementia paralytica formula," is applied to the humoral data encountered in cases of typical, ineffectively treated dementia paralytica. It denotes a clear, colorless aspect of the cerebrospinal fluid and certain results of the obligatory tests, which are stated.

If a dementia paralytica formula is detected, particularly in a case of asymptomatic neurosyphilis, the main task, according to the authors, is the selection of the most adequate form of therapy. For this decision, a consideration of the quantitatively different types of the dementia paralytica formula is indispensable. The resistance to antisyphilitic treatment parallels the strength of the dementia paralytica formula, which is best expressed by the total protein concentration. The authors suggest that the current qualitative concept of the dementia paralytica formula be abandoned and that the connection between this formula and its varying resistance to therapy on the basis of quantitatively different types be studied.

Frequent reference is made to the literature.

Management of chancroid in a tropical theater. E. M. Saltusky. J. A. M. A., Chicago, **127**: 259–262, Feb. 3, 1945.

The etiology, pathology, and clinical features of chancroid are briefly reviewed. The incidence of the disease in the United States Army personnel in various areas in 1917–1918 and during the present war is discussed. The incidence rate per thousand by months for chancroid and that for all venereal disease in the Army during 1942, 1943, and the first 4 months of 1944 are graphically compared. A routine for the management of the disease is given, based on the results of the treatment of 1,555 consecutive cases in an Army hospital.

The clinical symptoms of the disease are described, and the laboratory procedures necessary for the differential diagnosis are given. The literature concerning the laboratory tests for the diagnosis of chancroid is reviewed. In accordance with the instructions of the Surgeon General of the United States Army, the diagnosis in this series was not made on laboratory findings but on clinical grounds after other infections were ruled out by laboratory tests.

The therapeutic measures employed are detailed, including the method of local treatment of inguinal abscesses and the oral dosage of sulfonamides. The reactions caused by the oral sulfonamide therapy, all minor ones, are described.

All patients treated responded favorably. The average period of hospitalization was 11.2 days, whereas, in 1918, the average time lost from duty for chancroid in the

Army was 24.9 days.

The author concludes that further clinical and bacteriologic work is necessary for the more precise diagnosis of chancroid.

TREATMENT

Acute syphilitic meningitis treated with penicillin. Russell A. Nelson and Leroy Duncan. Am. J. Syph., Gonor. & Ven. Dis., St. Louis, **29:** 141–164, Mar. 1945.

Nelson and Duncan give a preliminary report of the effect of penicillin therapy on 10 patients with acute syphilitic meningitis.

The case history of each patient is reported in detail, and the results of clinical, serologic, and spinal fluid examinations in all patients are tabulated.

In 7 of the patients, the infection was of less than 8 months' duration; in 1, it was of 20 months' duration; in 1, indications were that it was of some years' standing; in 1, the onset could not be defined.

Four patients had had no previous antisyphilitic treatment, and 2 of these had associated mucocutaneous lesions of early syphilis. The other 6 patients had received treatment for early syphilis in varying amounts, consisting in 1 instance, of 60,000 units of penicillin. Except in case 8, the previous treatment was grossly inadequate. These 6 cases fell into the category of neurorecurrence.

Treatment consisted of intramuscular injections of sodium penicillin of 600,000 to 4,000,000 units given over a period of 7½ to 11 days.

Each of the 10 patients was observed over a period of 98 to 310 days after treatment. Immediate results were excellent from both clinical and laboratory standpoints. There was no evidence of clinical relapse in any patient, though 1 showed a relapse in the spinal fluid findings after 193 days.

Although penicillin does not appear in the cerebrospinal fluid after intramuscular injection, the authors conclude it is effective in acute syphilitic meningitis when administered by that route.

The treatment schedule advised for patients with acute syphilitic meningitis is a total dose of 2,000,000 to 3,000,000 Oxford units of penicillin administered intramuscularly every 3 or 4 hours, day and night for from 8 to 16 days. The authors consider intravenous injections relatively ineffective and intrathecal administration unnecessary. They recommend follow-up examinations at 3-month intervals during the first year, at 6-month intervals during the succeeding 2 or 3 years, and annually thereafter.

Administration of penicillin by mouth. Paul György, H. N. Vandegrift, William Elias, L. G. Colio, F. M. Barry and J. D. Pilcher. J. A. M. A., Chicago, **127:** 639–642, Mar. 17, 1945.

The authors report the results of investigations of the therapeutic efficacy and of the blood levels of penicillin when administered orally with and without sodium citrate.

To measure the therapeutic effect of the drug, observations were made on patients following therapy for various diseases, including gonorrhea and syphilis. Patients treated for gonorrheal infections included 18 male adults, 5 female children, and 3 infants with gonorrheal conjunctivitis. The majority of these patients were sulfonamide resistant. The doses administered varied from 10,000 units every 3 or 4 hours in children to 15,000 to 40,000 units every 3 hours in adults for 2 to 3 days, in combination with trisodium citrate (1 to 5 gm. per dose). In all of these cases apparent cure was achieved in 1 to 3 days. In 3 other cases (girls aged 2 to 5 years) prompt but only temporary clinical cure of the disease followed the treatment. After 2 repetitions of the same dosage followed by identical results, the same amount of the drug was given intramuscularly, and apparently permanent cure resulted.

In 1 patient with early acquired syphilis having a positive darkfield examination, the combined administration of penicillin (30,000 units every 3 hours) and sodium citrate (5 gm. per dose) by mouth did not differ in its result materially from

hat which ordinarily follows the parenteral administration of penicillin. Treponema pallidum decreased in number at 18 hours, and in 30 hours, darkfield examination was completely negative. At the end of the second day, however, the treatment was changed to intramuscular injections.

The blood level of penicillin in 2 groups of 12 patients each was measured following the oral administration of penicillin and sodium citrate. Given 30 minutes before breakfast, the dose increased the absolute blood levels and also prolonged the presence of penicillin in the blood, the drug being detected in the blood 4 hours after ingestion. Penicillin ingested after overnight fasting and 4 hours before the first meal gave less pronounced but significant results.

The following conclusions are stated:

1. Penicillin given by mouth in combination with a suitable buffer salt, such as trisodium citrate, was found to be therapeutically effective in a number of cases of gonorrhea and in one case of syphilis.

2. The effective doses were comparable to the doses routinely used in parenteral administration.

3. Combination of penicillin and sodium citrate given by mouth produces greater and more prolonged increase of penicillin blood levels than penicillin ingested without a buffer salt.

Toxic effects of arsenical compounds. T. J. Carter, Wesley M. Chambers and Laura T. Anderson. U. S. Nav. M. Bull., Washington, **44**: 195–207, Jan. 1945.

This article reports the arsenicals administered and the resulting toxic reactions, except arsenical dermatitis, observed among patients in the United States Navy during 1943. Comparative figures for the period 1925-1943 are also given.

The syphilis census of the Navy and Marine Corps as of Dec. 31, 1943 is given as 20,421, and this total is broken down into the numbers of patients who received each of the different arsenical or heavy metal compounds.

Deaths and severe reactions following the administration of neoarsphenamine during the years 1925-1943 and of mapharsen 1935-1943, and the ratios of deaths and severe reactions to doses are tabulated, as are the number of deaths following the use of 4 arsenicals from 1919 to 1943.

Case reports describing the treatment used for reactions following the administration of mapharsen and neoarsphenamine are given.

Fever therapy with intravenous foreign protein in neurosyphilis. D. C. Smith, J. C. Shafer and A. J. Crutchfield. South. M. J., Birmingham, **38**: 194–203, Mar. 1945.

The authors report on 90 patients treated from 1939 through 1943 with chemotherapy and hyperpyrexia induced by intravenous triple typhoid vaccine.

The equipment used is described as simple and available in any hospital. The bed is protected and insulated by a large rubber sheet over which is placed a cotton sheet. A light metal cradle from which is suspended a 100-watt light bulb protected by a screen is then placed on the bed. The cradle is covered by blankets and a rubber sheet large enough to be tucked in at the sides and foot of the bed and to cover the patient's shoulders. Several layers of blankets are placed about the head and shoulders so that only the face is exposed. The patient is thus free to move and can cooperate with such routine care as temperature taking. Control of elevation of temperature was effected by turning off the electric light and loosening the pack about the cradle.

About 750 episodes of fever were given with only minor reactions except in 1 case: that of a white man, aged 40, with moderately advanced paresis and a hypertension of 175/92. An excessive amount of vaccine was inadvertently given the patient when his temperature was elevated to 101°; "heat stroke" developed and the patient died the same day.

Arsenicals administered at the height of the fever included arsphenamine, mapharsen, and clorarsen. There were no untoward reactions. The cradle and light technic was so developed that the total hours of fever were definitely prolonged.

A summary is given of clinical results in 19 patients with acquired paresis: 57.9 percent were greatly improved and returned to their preparetic level; 26.3 percent were improved; they were able to work and gave evidence of fair social adjustment. One patient had to be institutionalized but at last report was soon to be discharged. Only 15.8 percent of the patients was unimproved or showed progression; therefore, 84.2 percent of the 19 cases showed either marked or moderate clinical improvement.

Case histories for a number of patients and an abstract of discussion are given.

Treatment of gonorrhea and studies of intramuscular irritation. Lawrence E. Putnam, Henry Welch and Sidney Olansky. J. A. M. A., Chicago, **127**: 204–205, Jan. 27, 1945.

The purpose of the investigation reported in this paper was to study the irritation caused by injections of each of 7 salts of penicillin.

Thirty-five patients with sulfonamide resistant gonorrhea were treated with intramuscular injections of 7 salts of penicillin, 5 patients with each of the following: sodium, lithium, ammonium, strontium, calcium, magnesium, and potassium. Since it had already been shown that the toxicity of these preparations in mice depends upon the cation used in their production, each salt was assayed chemically to determine the weight of cation present, and in no case was the amount in 100,000 units sufficient to contraindicate its use in man. The treatment consisted of the injection of 100,000 units of penicillin dissolved in 20 cc. of isotonic solution of sodium chloride in 4 equal doses at 3-hour intervals. The injections were made at 3 different muscle sites, gluteal, triceps, and deltoid. In the group of patients were 23 females, 8 white and 15 Negro, and 12 males, all Negro. They varied in age from 14 to 44 years.

In an attempt to correlate the amount of pain produced in man with objective evidence of irritation in rabbits, injections of from 2,000 to 10,000 units of the same penicillin salts in 5 cc. of distilled water were made in rabbits.

The following conclusions were reached:

All the patients were cured, as evidenced by negative cultures taken on the first, third, and fifth days after treatment. Only one penicillin preparation, penicillin ammonium, produced severe pain on intramuscular injection in man. Intradermal injections of this preparation produced a hemorrhagic reaction in rabbits. All the other salts produced only slight to moderate edema in rabbits within 1 to 2 hours after injection. Injections into the buttock caused less pain than injections into the triceps or deltoid muscles.

LABORATORY RESEARCH

The relative activity of partially purified penicillin and of crystalline penicillin G on Treponema pallidum. Wolcott B. Dunham and Geoffrey Rake. Am. J. Syph., Gonor. & Ven. Dis., St. Louis, **29**: 214–228. Mar. 1945.

The authors report the results of experiments performed in vitro and in vivo to determine the relative activity of partially purified penicillin and of crystalline penicillin G on Treponema pallidum.

The methods and materials used are described.

It is suggested that some of the therapeutic effects produced by impure penicillin but not by crystalline penicillin G may be due to the presence of other penicillins or of impurities. To test this theory, experiments are under way to determine the relative activity of other forms of penicillin in rabbits.

The following conclusions are stated:

1. Crystalline penicillin G has very little or no effect on the motility of T. pallidum when the latter are exposed to 8,800 u./ml. for two hours in vitro.

2. Under the same conditions, a solution containing 2,200 u./ml. of the least pure penicillin preparation employed in these studies immobilizes all of the spirochetes.

3. A substance in partially purified penicillin that immobilizes spirochetes can be concentrated by adsorption on alumina and recovered by elution.

4. The concentration of the substance in partially purified penicillin that is active against spirochetes in vitro is only very slightly, if at all, reduced by incubation at 37° C. in the presence of a weak solution of penicillinase over a period of eleven days, conditions under which a large proportion of the penicillin present is inactivated. The immobilization of spirochetes in vitro by partially purified penicillin is due, therefore, to one or more of the impurities present.

5. No marked degree of immobilization is produced by solutions containing 3.5 mg./ml. of penillic acid or 3.0 mg./ml. of a product of the hydrolysis of pure penicillin G.

6. Spirochetes exposed to 1,100 u./ml. of certain partially purified preparations of penicillin are noninfectious for rabbits when injected intratesticularly, although many of them are still motile at the time of injection. Spirochetes similarly exposed to 8,800 u./ml. of crystalline penicillin G produce orchitis in rabbits.

7. Partially purified penicillin, 330 u./mg., protected a large proportion of rabbits from local and generalized infection when 66,000 units per kilogram of body weight were administered intramuscularly in the leg five hours after a suspension of spirochetes had been rubbed into an incision in the skin of the back. The same dose of crystalline penicillin G in another experiment failed to protect.

8. The injection of 166,000 u./kg. of crystalline penicillin G prevented the development of local syphilitic lesions in a large proportion of the rabbits. This demonstrates that crystalline penicillin G has an antisyphilitic action.

9. In the same experiment, however, an alumina adsorbate of partially purified penicillin showed a greater activity in vivo than did crystalline penicillin G.

10. These experiments in rabbits indicate that, because of the large quantity that would be required, it would not be practicable at the present time to employ penicillin in a single dose, administered systematically, as a prophylactic against syphilis in human beings.

Interaction between crystalline penicillin and human plasma proteins. Bacon F. Chow and Clara M. McKee. Science, Lancaster, 101: 67–68, Jan. 19, 1945.

The authors report the result of experimental studies carried out in an attempt to determine whether penicillin will combine with human plasma protein.

Seven milliliters of buffered solutions of human alpha, beta, or gamma globulin or of human serum albumin containing 125 micrograms of crystalline sodium salt of penicillin per ml. were put into cellophane bags and equilibrated with 14 ml. of a phosphate buffer solution of penicillin of the same concentration and pH. After 18 to 24 hours of continuous rocking at 1° C., the concentrations of the penicillin in the plasma and in the surrounding dialysate were determined.

So far as testing would reveal, there was no demonstrable union between penicillin and any of the globulins. Approximately two-thirds of the penicillin in the albumin mixture became nondialyzable, a result assumed to be due to the physical or chemical union of the penicillin and albumin molecules.

The penicillin-albumin complex was isolated by precipitation in an aqueous 50 percent alcohol solution at 5° C., a solution in which unbound penicillin is soluble. The new compound was obtained in a dried powder form by lyophylization.

If the compound is the result of a chemical union, the complex is expected to be more slowly excreted by experimental animals and by patients than unbound penicillin because of the increased size of the molecule. It has been found that mice receiving intramuscular injections of the solution did not excrete the drug as rapidly as did mice receiving the same dose of free penicillin by a similar route.

Since the protein used is normal human albumin, it is expected that the resulting compound will be nontoxic and nonantigenic for man. Its metabolism, its im-

munologic properties, and its stability toward acid, alkali, and penicillinase will be reported after studies have been completed.

The effect of sodium hydroxide on biologic falsely positive and anticomplementary serologic reactions in syphilis. Herman Brown, John A. Kolmer and Elsa R. Lynch. Am. J. Syph., Gonor. & Ven. Dis., St. Louis, 29: 200–213. Mar. 1945.

The authors report the results of an investigation of a method whereby the reagin responsible for false positive reactions to the test for syphilis occurring in individuals with certain diseases could be inactivated or destroyed without inactivating or destroying the syphilis reagin.

The method used, which is described in detail, consisted of pretreating the serum chemically by the addition of N/3 or N/4 solution of sodium hydroxide and by heating. Results are given following its application to normal rabbit serum and that of nonsyphilitic human beings with malaria, infectious mononucleosis, leprosy, virus pneumonia and certain other diseases, as well as syphilis.

The method proved effective in preventing biologic falsely positive Kolmer, Kahn, and Mazzini reactions in serums of normal rabbits and in a large percentage of serums of presumably nonsyphilitic individuals with malaria and infectious mononucleosis. In each of these serums, N/3 sodium hydroxide was more effective than the N/4 solution. Less effective results were observed with the serums of presumably nonsyphilitic lepers, and in leprosy, the N/4 solution was found to produce results superior to those following the use of N/3 sodium hydroxide.

It was found that this treatment applied to syphilitic serums resulted in the inactivation or destruction of some syphilis reagin, but according to the authors, falsely negative Kolmer complement fixation reactions are likely to occur only in the case of serums containing small amounts of reagin.

Furthermore, the addition of N/3 or N/4 sodium hydroxide to rabbit and human serums has prevented the occurrence of anticomplementary reactions in the Kolmer complement fixation test. There was some loss of syphilis reagin, but again the authors note that falsely negative reactions are not likely to occur except in the case of serums containing small amounts of reagin.

An experimental investigation of the etiology and immunology of granuloma inguinale. Katherine Anderson, W. A. DeMonbreun and E. W. Goodpasture. Am. J. Syph., Gonor. & Ven. Dis., St. Louis, 29: 165–173, Mar. 1945.

This paper presents a summary of experiments carried out during the past two years in which a microorganism having morphologic identity with the Donovan body and specific antigenic relationship to patients with granuloma inguinale has been isolated and cultivated in the yolk of developing chick embryos.

The authors' summary of their findings follows:

1. The same microorganism has been isolated from the lesions of 3 patients with granuloma inguinale.

2. The Donovan microorganism has not become cultivable on ordinary artificial culture media, on the chorioallantois of chick embryos, in the yolk of infertile eggs, nor is it pathogenic for mice, dogs, M. rhesus monkeys, rabbits or chickens.

3. Embryonic yolk in vitro supports the growth of the microorganism.

4. Washed bacterial bodies stimulate an apparently specific cutaneous reaction in the skin of patients with active granuloma inguinale.

5. A "capsular" substance soluble in N/100 NaOH is precipitable from infected yolk with N/100 HCl.

6. This "capsular" substance gives an apparently specific precipitation reaction in patient's serum. It fixes complement in patient's serum and stimulates a mild skin reaction in the skin of patients with granuloma inguinale.

7. In our opinion, these experiments describe a culture medium suitable for the growth of the Donovan body which has

therto not been cultivated outside the dy of the human host. They determine nat seems to be the bacterial nature of e etiologic agent of granuloma inguinale, d afford an avenue of approach to the lution of the isolation of its obligate owth factor, and the refinement of use- l aids to diagnosis.

se of the yolk sac of the developing chicken embryo in the isolation of the agent of lymphogranuloma venereum. Morris F. Shaffer, Helen Jones, Arthur W. Grace, Dorothy M. Hamre and Geoffrey Rake. J. Infect. Dis., Chicago, **75**: 109–112, Sept.-Oct. 1944.

This paper describes the isolation of 2 rains of the agent of lymphogranuloma nereum by inoculation directly from a man patient to the yolk sac of a fertile g. It was believed that the chick embryo veloping within the protection of the shell ould be an ideal experimental animal for e in isolating this organism. It is possible at the agent isolated from human lymphoanulomatous material inoculated into onkeys or mice, the animals commonly ed, may be derived from the animal and nce does not represent the etiologic gent of the human disease. The use of e yolk sac would eliminate the possibility confusion of the agent with another ember of the same group of agents, 8 of hich are known to cause infections in imal species.

Suspensions of pus from the inguinal iboes of 2 human patients were inoculated rectly into the yolk sacs of embryonated icken eggs, and 2 strains, H. H. and /. W., were isolated. In only one of the iaracteristics so far examined have these strains differed from one another. Brain id spleen pools from the mice which 3 eeks earlier had received W. W. yolk sac spensions intravenously were inoculated to the yolk sac of normal embryos. In is way 7 carriers were found in 10 mice sted. With the previously described strain, H., no carriers were found in 18 mice ter intravenous inoculation of these imals.

In sulfonamide susceptibility, tissue tropisms, and type of endotoxin produced, these strains isolated by the yolk sac technic resemble the other strains of the agent of lymphogranuloma venereum with which the authors have worked; in the 3 latter characteristics they differ from strains of all other members of this group. These characteristics seem to be so constant for all strains of a given agent in this group that a study of the 3 would seem to be sufficient to distinguish among those members of the lymphogranuloma-psittacosis group so far recognized.

Optimal carbon-dioxide tensions for primary isolation of the gonococcus. William Ferguson. Am. J. Syph., Gonor. & Ven. Dis., St. Louis, **29**: 19–55, Jan. 1945.

The present study was undertaken for the purpose of defining more exactly than has heretofore been done the carbon dioxide requirements of gonococci during primary isolation, and also of examining the effect of gaseous environments other than carbon dioxide upon the growth of gonococci.

The materials and technics used are described in considerable detail.

The author summarizes his findings as follows:

1. By gas analysis it was established that approximately 2.3 percent of carbon dioxide is furnished by burning a candle in a closed container of 6 liters capacity.

2. By plate count of strains from acute male cases of gonorrhea, it was found that equal growth of gonococci occurs in a jar in which a candle furnishes carbon dioxide, and in a jar whose atmosphere is enriched with 10 percent carbon dioxide.

3. An increase in atmospheric moisture content was found to stimulate growth of aerobic strains of the gonococcus.

4. In all the experiments in which a comparison was made of the efficacy of atmospheric air, reduced oxygen tension produced by partial vacuum and air reinforced with carbon dioxide, the latter condition was found to produce the best growth of gonococci.

5. Primary strains of the gonococcus

were found to grow equally well on chocolate agar in a zone of carbon dioxide enrichment with a lower limit between 2 and 2.3 percent and an upper limit between 18 and 22 percent.

6. A moderate growth of gonococci was obtained in percentages of carbon dioxide as high as 40 percent. The morphology of the organism was considerably changed by growth under high concentrations of this gas.

7. Hydrogen, carbon monoxide, and nitrogen gases in concentrations of 10 percent in air did not contribute growth stimulation to gonococci.

Development in vitro of penicillin-resistant strains of the gonococcus. Jeanne M. Bahn, Helen Ackerman and Charles M. Carpenter. Proc. Soc. Exper. Biol. & Med., Utica, 58: 21–24, Jan. 1945.

The present study was undertaken to determine if the gonococcus when grown in the presence of gradually increased concentrations of penicillin acquires resistance in vitro.

Five strains of gonococci nonresistant to sulfanilamide and sulfathiazole were selected for the study. Cultures were transferred to the same and to a greater concentration of penicillin every 48 hours for 32 weeks, and subcultures for viability were made on chocolate agar plates at the same interval but on alternate days. Weekly tests were made of each strain on a suitable carbohydrate medium to determine if any change in fermentation reactions had occurred. Two strains most resistant to penicillin in vitro were maintained on chocolate agar and also were lyophilized by the technic of Flosdorf and Mudd to determine if the acquired resistance were transient or permanent.

Results showed that all 5 strains of the gonococcus were made resistant in vitro to concentrations of penicillin. Morphologic changes of the gonococcus that were apparently temporary and a delayed fermentation of glucose were observed in the strains during the development of resistance to the drug.

Technique of the standard Kahn te and of special Kahn procedure Reuben L. Kahn. Univ. Michiga Press, Ann Arbor, Mich., Oct. 1944.

This 52-page bulletin is intended to ser as a practical guide to the technics of tl various serologic tests devised by Kal for the examination of serum and of spin fluid. It also outlines the methods of inte preting and reporting these tests. Includ are the standard diagnostic test, presum tive test, quantitative test, verification te and microflocculation procedures, togeth with an appendix on the preparation ar standardization of antigen. For the pri ciples underlying the procedures and ela orate discussions of the various steps er ployed the reader is referred to the san author's larger publication, "The Kal Test—A Practical Guide."

The bulletin is a useful manual for tho engaged in laboratory work.

PUBLIC HEALTH ADMINISTRATION

Nonmedical venereal disease control o ficers. Medicine and the war. J. A M. A., Chicago, 127: 465, Feb. 2 1945.

The Navy will commission 50 no medical venereal disease control officer according to plans recently announce Under Special Program No. 166 of tl Bureau of Naval Personnel, these office will be assigned to various Naval activiti to conduct educational programs in venere disease control under the direction of tl activity's medical officer. They will act liaison officers with civilian health author ties in the area to which they are assigne establish community relations, lecture the causes of venereal diseases and how avoid them, and keep statistical records venereal disease control work in the respective districts. They will not admini ter treatment.

The required qualifications are stated.

New Cases of Syphilis and Gonorrhea in States, Territories and Possessions

Health Officers' monthly statement: Reported for the first 8 months of fiscal years 1944-45 and 1943-44

Area	Cases of syphilis and gonorrhea reported for first 8 months of fiscal years below:											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44
Total United States...	229,787	311,319	49,870	52,004	64,020	83,542	92,464	137,197	7,715	8,951	181,977	201,787
Alabama	8,221	11,650	1,203	1,562	1,769	2,679	1,665	2,730	188	245	4,288	4,334
Arizona	1,194	1,853	355	432	358	504	379	725	90	87	770	1,139
Arkansas	7,896	6,735	2,044	841	2,668	2,250	2,582	2,597	215	144	4,336	3,033
California	18,656	21,561	3,386	3,473	4,240	5,013	10,103	12,048	556	639	19,618	22,023
Colorado	1,725	2,787	461	678	506	790	693	1,212	65	107	1,525	2,219
Connecticut	1,591	1,895	168	224	750	838	331	480	51	71	815	1,046
Delaware	385	634	92	94	118	161	139	145	16	9	144	147
Dist. Columbia	2,668	5,556	612	639	825	1,316	1,049	3,349	66	90	3,461	2,516
Florida	10,338	19,330	1,279	2,189	3,865	6,090	4,302	8,800	284	406	8,686	10,839
Georgia	7,035	10,537	1,974	2,068	2,808	4,249	2,033	3,904	214	311	5,281	6,778
Idaho	534	356	100	162	145	61	259	102	20	5	300	547
Illinois	14,500	18,483	2,448	2,495	3,459	4,243	8,177	11,377	416	368	13,673	15,651
Indiana	4,232	5,828	891	886	549	530	1,440	2,144	134	163	1,783	2,463
Iowa	1,073	1,639	247	319	328	432	409	710	49	110	1,573	1,195
Kansas	1,743	1,918	425	391	312	405	939	1,052	67	70	1,608	1,264
Kentucky	3,401	4,754	897	751	783	1,032	1,200	2,002	158	181	3,302	2,364
Louisiana	7,333	11,870	1,684	1,987	2,174	3,062	1,775	3,109	298	298	6,699	9,120
Maine	532	589	102	130	64	86	229	290	43	48	1,048	899
Maryland	5,524	9,851	1,147	1,094	1,320	1,045	1,437	1,909	115	83	3,123	4,807
Massachusetts	2,712	3,726	639	764	(§)	(§)	1,924	2,748	149	212	2,652	3,358
Michigan	11,335	11,322	2,112	1,673	3,215	2,920	4,135	4,833	276	283	7,947	7,423
Minnesota	1,262	1,629	197	156	122	174	858	1,187	47	81	1,534	1,290
Mississippi	13,257	17,311	4,526	5,874	3,969	4,852	4,053	5,868	709	713	19,915	19,738
Missouri	6,024	6,855	1,321	1,176	1,710	1,764	2,583	3,323	204	224	4,940	3,846
Montana	285	283	59	71	25	49	83	114	7	5	190	208
Nebraska	901	843	138	127	251	398	458	256	34	24	968	1,000
Nevada	237	487	59	15	6	94	86	336	8	17	481	249
New Hampshire	196	162	23	23	34	37	120	86	14	7	119	131
New Jersey	5,288	7,394	799	866	1,432	2,272	2,772	3,943	220	294	2,997	3,615
New Mexico	1,121	1,303	244	269	312	302	500	671	79	60	847	955
New York	20,744	24,488	4,212	3,542	4,307	4,285	11,489	15,678	549	672	9,832	12,860
North Carolina	5,629	7,525	2,083	1,952	2,138	3,078	1,306	2,365	102	130	5,850	5,979
North Dakota	129	206	27	71	18	33	52	58	8	13	221	177
Ohio	12,496	15,394	2,697	2,398	3,429	3,713	5,854	7,889	494	613	4,154	3,633
Oklahoma	4,938	5,298	798	699	1,302	1,495	1,590	1,940	177	199	5,305	3,392
Oregon	1,274	1,357	346	418	148	108	718	786	50	45	1,644	1,662
Pennsylvania	7,413	8,898	1,341	1,188	2,502	3,368	2,445	3,301	308	442	0	614
Rhode Island	570	703	128	56	52	73	293	502	24	17	821	504
South Carolina	5,211	10,849	1,563	2,189	1,686	4,384*	1,577	3,768	193	264	4,358	4,509
South Dakota	271	340	41	63	76	60	122	164	26	27	322	255
Tennessee	8,701	12,611	1,545	1,638	3,346	5,091	3,333	5,458	292	272	7,930	9,725
Texas	8,909	16,983	2,016	2,104	3,175	5,163	2,896	7,030	334	503	6,396	7,330
Utah	357	569	106	143	37	74	304	340	10	12	349	409
Vermont	118	169	16	54	33	51	45	56	11	7	262	135
Virginia	6,198	9,915	1,872	2,820	2,488	3,760	1,573	3,010	201	183	3,715	8,296
Washington	2,532	2,921	545	590	602	634	1,041	1,297	52	91	3,434	5,723
West Virginia	1,605	2,484	640	456	256	407	393	586	46	79	1,956	1,529
Wisconsin	547	625	126	118	3	0	407	500	11	7	681	729
Wyoming	946	843	136	76	305	117	413	419	35	20	124	129
Alaska	68	65	22	39	17	13	14	10	1	1	326	297
Canal Zone	523	(*)	63	(*)	103	(*)	298	(*)	15	(*)	392	(*)
Hawaii	402	641	101	120	51	74	220	446	22	39	782	1,137
Puerto Rico	6,678	10,073	955	1,046	2,304	1,980	1,860	3,349	1,453	1,288	4,017	2,513
Virgin Islands	(*)	145	(*)	26	(*)	86	(*)	26	(*)	6	(*)	219
Total U. S. and Possessions	237,458	322,243	51,011	53,235	66,495	85,695	94,856	141,028	9,206	10,285	187,494	205,953

* Data not available
** Includes "not stated"
§ Included in late latent

New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over

Health Officers' monthly statement: Reported for the first 8 months of fiscal years 1944-45 and 1943-44

City	Cases of syphilis and gonorrhea reported for first 8 months of fiscal years below:											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44
Total†	[1]85,593	[1]112,327	[2]16,865	[2]13,039	[2]20,326	[2]24,335	[2]38,675	[2]50,387	[2]2,092	[2]2,089	[1]62,876	[1]54,132
Akron	637	574	174	79	148	140	278	308	37	33	417	211
Atlanta	1,725	1,812	483	456	498	567	709	880	35	20	1,969	796
Baltimore	3,839	7,822	956	843	939	747	1,231	1,514	46	47	2,009	1,868
Birmingham	1,782	3,193	257	225	445	876	467	780	46	55	473	397
Boston	1,015	1,204	236	235	80	0	556	774	43	30	981	884
Buffalo	1,105	1,346	167	157	152	161	752	995	34	33	760	592
Chicago	10,054	10,419	1,809	1,695	2,583	2,469	5,423	6,050	239	205	9,640	8,762
Cincinnati	1,543	2,036	256	271	0	0	1,287	1,765	0	0	752	662
Cleveland	2,768	2,731	564	502	880	887	1,270	1,278	54	64	1,196	1,018
Columbus	921	1,065	293	218	204	234	386	565	38	28	324	225
Dallas	(*)	1,699	(*)	318	(*)	345	(*)	1,023	(*)	12	(*)	492
Dayton	710	1,193	88	135	270	336	330	685	22	37	345	492
Denver	826	1,361	223	305	259	363	298	506	27	41	834	1,222
Detroit	6,459	7,988	1,336	1,028	2,252	2,434	2,749	4,384	122	142	3,753	3,878
Honolulu	158	346	31	45	20	43	93	229	9	29	551	758
Houston	1,128	1,291	259	209	442	460	383	586	44	36	1,385	1,512
Indianapolis	1,363	1,513	288	386	155	52	299	372	24	19	390	70
Jersey City	246	344	30	35	79	75	123	226	14	18	62	29
Kansas City	900	1,214	173	206	229	228	435	731	39	45	697	647
Los Angeles	6,950	7,387	1,823	0	399	2,923	4,524	4,251	204	213	4,492	3,355
Louisville	843	1,410	282	245	174	257	334	585	23	15	1,055	602
Memphis	3,807	4,584	511	395	1,800	2,152	1,355	1,971	141	66	3,531	3,661
Milwaukee	354	335	57	32	19	5	274	283	5	2	260	121
Minneapolis	398	462	97	72	67	80	223	298	11	10	726	530
Newark	1,155	1,523	228	190	380	400	527	884	30	49	841	595
New Orleans	987	1,855	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,074	1,383
New York	14,989	16,964	3,434	2,999	3,728	3,795	7,349	9,558	368	405	9,832	9,209
Oakland	1,190	1,012	164	120	307	247	623	605	33	30	1,281	927
Oklahoma City	(*)	1,306	(*)	133	(*)	351	(*)	408	(*)	32	(*)	648
Omaha	353	374	65	34	77	200	200	113	11	18	306	328
Philadelphia	4,043	6,648	523	226	888	716	1,158	860	111	52	758	599
Pittsburgh	984	6,177	184	(*)	259	(*)	487	(*)	54	(*)	240	88
Portland	(*)	578	(*)	164	(*)	34	(*)	370	(*)	10	(*)	721
Providence	305	343	42	52	34	31	172	226	10	6	125	111
Rochester	199	182	40	34	16	14	140	130	3	4	268	189
St. Louis	3,896	4,097	795	534	1,242	1,359	1,744	2,067	115	127	2,795	1,336
St. Paul	156	194	21	24	25	31	90	123	8	9	177	196
San Antonio	773	812	92	110	152	212	416	453	19	28	701	921
San Diego	833	777	124	70	232	225	338	422	30	27	740	607
San Francisco	1,710	1,971	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,852	1,427
Seattle	1,030	908	223	117	275	161	510	5.3	15	15	1,391	1,10(
Syracuse	411	664	46	19	17	21	308	6 7	5	17	311	21(
Toledo	380	640	63	97	34	118	272	401	11	24	121	8(
Washington, D. C.	2,668	5,556	612	639	825	1,316	1,049	3,349	66	90	3,461	2,51(
Actual total‡	85,593	115,910	17,049	13,654	20,585	25,065	39,162	52,188	2,146	2,143	62,876	55,99

* Data not available
** Includes "not stated"
† Based on cities reporting in both fiscal periods
‡ Includes all reported cases
[1] Based on 41 cities
[2] Based on 38 cities

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